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Childhood trauma and social stress reactivity in psychosis

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Symposium Session 1

Thursday, October 20

1:00–2:30 p.m., Washington A

Fidelity and Quality Measures for First Episode Psychosis Services

Chair: Masafumi Mizuno¹, Co-Chair: Merete Nordentoft²

Speakers: Donald Addington, Peter B. Jones, Marianne Melau, David McDaid

¹Department of Neuropsychiatry, Toho University School of Medicine, Tokyo, Japan, ²Copenhagen University Hospital, Copenhagen, Denmark

The Board of the IEPA Early Intervention in Mental Health decided at its 2014 Annual Meeting in Tokyo to convene a Fidelity Task Force comprised of an international group of experts to review the current state of implementation of early psychosis services and focus on tools such as fidelity scales and performance measures that can be used to support broader implementation of services. The Task Force met in December 2015 to establish the framework of a paper which was then developed and reviewed at a second meeting in April 2016. In this symposium, we will summarize the key principles underlying first episode psychosis services, examine the application of fidelity scales and outcome measures to support implementation of evidence based practices in mental health and review fidelity scales developed for first episode psychosis services.

Talk 1

Fidelity and Quality Measures for First Episode Psychosis Services

Donald Addington¹, Maximilian Birchwood², Peter Jones³, Eóin Killackey⁴, David McDaid⁵, Marianne Melau⁶, Masafumi Mizuno⁷, Kim Mueser⁸

¹University of Calgary, Alberta, Canada, ²Mental Health and Wellbeing, Warwick Medical School, Coventry, UK, ³University of Cambridge, Cambridge, UK, ⁴Orygen, The National Centre of Excellence in Youth Mental Health, The University of Melbourne, Parkville, Australia, ⁵London School of Economics and Political Science, UK, ⁶Copenhagen University Hospital, Copenhagen, Denmark, ⁷Department of Neuropsychiatry, Toho University School of Medicine, Tokyo, Japan, ⁸Boston University, Boston, Massachusetts, USA

Aim: First Episode Psychosis Services are evidence based practices which improve the outcome of a first episode of psychosis and the early stages of schizophrenia. Fidelity and outcome measures are important tools for maintaining quality and fostering widespread program implementation. The purpose of this paper is to review fidelity and outcome measures which can be used to broaden implementation of first episode psychosis services and ensure quality of existing services.

Methods: We reviewed the general principles and essential evidence based components that underpin first episode psychosis services in order to establish measurement targets. We reviewed implementation of such services internationally, the availability of reliable and valid fidelity measures and outcome indicators and the economic barriers to implementing both services and quality measures.

Results: Early Psychosis Services are variably offered in high-income countries and rarely with attention to access and quality of services. They are not available in middle and low income countries. Reliable and feasible measures of access, fidelity and outcome exist but system wide barriers to quality assessment in mental health services impede their application.

Conclusions: Reliable tools now exist to assess quality and access to early psychosis services and support implementation.

Talk 2

Cost-effectiveness of Fidelity in Early Intervention For Psychosis: How Good is Good?

Peter B. Jones¹, M Radhakrishnan, P McCrone, L Lafortune, L Everard, D Fowler, T Amos, N Freemantle, SP Singh, M Marshall, V Sharma, M Birchwood

¹Department of Psychiatry and NIHR CLAHRC EoE, Cambridge, UK

Background: International implementation of Early Intervention Services (EIS) for psychosis requires evidence about the components providing good value for money. Aims To assess the cost-effectiveness of EIS according to the English Department of Health 2001 Policy Implementation Guide (PIG), and contrast this with a new waiting time target (2 weeks) and standard (AWTTS; 50% meeting the 2-week target) beginning April 2016.

Methods: National Eden Study data were assessed for cost-effectiveness at a threshold of £20,000 per QALY after classifying sites into three fidelity groups: 75-80 % (high), 81%-90% (very high), and 91-95 % (virtually complete). This was contextualised against the AWTTS.

Results: The very high (middle) fidelity group had a 56.3% likelihood of being the most cost-effective followed by high fidelity (35.8%) and the virtually complete fidelity services (7.9%). The AWTTS focuses on intervention delivery (CBTp, antipsychotic drugs and family interventions). Workforce requirements and stopping-the-clock only on acceptance by team capable of delivering these interventions mean team structure remains important.

Conclusions: Striving to maximise fidelity may not be warranted in the short-term, but dropping below a certain level of fidelity may be inefficient. Implementation of policy at a national level needs to incorporate nuance. Declaration of interest None

Talk 3

Program Fidelity of Specialized Early Intervention Services in Denmark

Marianne Melau, Nikolai Alberts, Merete Nordentoft

Copenhagen University Hospital, Copenhagen, Denmark

Background: The Specialized Early Intervention (SEI) treatment in Denmark, the OPUS treatment, has in a randomized clinical trial proved to be effective compared to treatment as usual, and the dissemination of SEI services are increasing in Denmark. A prerequisite for upholding positive effects and preserving the critical components from the original concept is to ensure fidelity to model adherence. A fidelity scale is an effective tool to assess elements critical to the SEI programme tested.

Method: In order to develop a Danish fidelity scale, we identified essential evidence-based components of SEI services internationally and interviewed experts from Danish SEI-teams, using an adapted version of the Delphi Consensus method. An 18-point scale was conducted, of which 5 of the components are mandatory. The scale was divided into two dimensions: one concerning the structure and the other concerning the character and content of the treatment. The assessment of the scale is based on interviews with team leaders, with selected patients and staff members, medical records, and by observing a team meeting. This multimodal approach makes the most valid assessment. Alongside the assessment of fidelity we will record characteristics of each team and their specific patient populations.

Result: Fidelity data will be collected from 21 SEI teams all over Denmark. Data will be ready for presentation at the fidelity-symposium.

Conclusion: If testing the fidelity scale proves positively, it can easily be implemented in practice and will have profound implications for patients and their relatives by ensuring quality of the treatment they are offered.

Talk 4

International Implementation of Early Intervention Services: Analysis of Economic and Health System Barriers and Facilitators

David McDaid, A-La Park, Valentina Iemmi, Martin Knapp

London School of Economics and Political Science, UK

Aims: While first episode psychosis services have been developed in very different health systems, there are marked differences in service availability, despite evidence on their effectiveness and cost effectiveness. This presentation extends on a previous review of the development of these services in high income country contexts, identifying economic and health system barriers and facilitators to their implementation.

Methods: A systematic literature review was undertaken to map and identify early intervention services around the globe. In addition, funding mechanisms, as well as measures to enhance and monitor access and quality were analysed. This was done through bibliographic databases, triangulated with information from government and working papers, websites and video documentation.

Results: Significant service provision with sustainable mainstream funding is restricted to a handful of high-income health systems; most programmes remain reliant on research funding with limited coverage and reach. The content and structure of services also varies substantially, including recent efforts to address resource and capacity limitations by expanding the remit and skills of existing community mental health services rather than through creation of stand-alone services. There has been little evaluation of the costs and effectiveness of mechanisms to encourage implementation.

Conclusions: It is important to understand how differing health system structures and incentives impact on the development of first episode psychosis services. Measures to align financial and other incentives within and beyond the health system, as well mechanisms

to monitor fidelity in service delivery may help future implementation.

Question and Answer Period

Discussant: Mirella Ruggeri, University of Verona, Italy

Symposium Session 2

Thursday, October 20

1:00–2:30 p.m., Washington B

Management of Psychosis Without the Use of Antipsychotic Medication

Chair: Patrick McGorry M.D., Ph.D.^{1,2}, Co-Chair: Brian O'Donoghue^{1,2}

Speakers: Philippe Conus, Shona Francey, Brian O'Donoghue, Anthony Morrison

¹Orygen, The National Centre of Excellence in Youth Mental Health, Centre for Youth Mental Health, ²Centre for Youth Mental Health, University of Melbourne, Parkville, Australia

The establishment of Early Intervention for Psychosis Services has led to a reduction in the delays in treatment for young people with psychotic disorders and more specialized treatments. With the substantial reductions of the duration of untreated psychosis now seen in many early psychosis services, based on the staging model and stepped care principles, it may be that the immediate introduction of antipsychotic medication may not be necessary. Additionally, a proportion of young people with a first episode of psychosis (FEP), with decisional capacity, elect not to take antipsychotic medication. There is a dearth of information on what other interventions may benefit this group. This symposium aims to address the important and topical question of whether psychotic disorders can be managed without the use of antipsychotic medication. Dr Philippe Conus will present outcome data for those who were not treated with an antipsychotic medication from a large, naturalistic, representative FEP cohort. Dr Shona Francey will describe the study protocol for the STAGES study, an RCT of intensive psychosocial interventions + - antipsychotic medication in early psychosis and baseline characteristics of participants. Dr Brian O'Donoghue will describe the safety measures and outcomes of conducting the STAGES study. Prof Anthony Morrison will present findings of the ACTION trial, an RCT of cognitive therapy in individuals with a diagnosis of schizophrenia who have elected not to take antipsychotic medication. Prof Morrison will also describe the progress of an ongoing RCT evaluating cognitive therapy in comparison to antipsychotic medication or a combination of both.

Talk 1

Can We Predict Good Outcome Among Patients Who Refuse Medication? – Results From the FEPOS Study

Philippe Conus¹, Sue Cotton², Benno Schimmelmann¹, Patrick McGorry², Martin Lambert³

¹DP-CHUV, Lausanne University, Lausanne, Switzerland, ²PEDIC, University Medical Center Hamburg-Eppendorf, Germany, ³Orygen, The National Centre of Excellence in Youth Mental Health, Centre for Youth Mental Health, University of Melbourne, Parkville, Australia

Background: The literature suggests that some first episode psychosis (FEP) patients can have good outcome without antipsychotic medication. However, there is very limited evidence on which a choice of treatment without antipsychotic can be based.

Methods: FEPOS is a file-based study of an epidemiological sample of 704 FEP patients treated at EPPIC, Melbourne, between 1998 and 2000. Among the 661 patients where data was available, 108 consistently refused medication during the entire duration of their treatment at EPPIC. In this paper we compared, within this sub-group, patients who had a favourable outcome with those who did not.

Results: Patients were aged between 15–29 years ($M = 21.9$, $SD = 3.40$) and the majority were male (70.4%, $n = 76$). Symptomatic remission data was available on 105 patients; of these patients 41.0% ($n = 41$) had achieved remission. Functional remission data was available on 100 patients; of these patients 33.0% ($n = 33$) had achieved functional remission. Combined remission was evident in 23.0% ($n = 23$) of patients. Three factors were associated with symptomatic remission: better premorbid functioning (based on GAF, $OR = 1.07$, $p = .006$), higher number of years of education ($OR = 1.43$, $p = .020$), and being employed or studying at service entry ($OR = 2.59$, $p = .034$). Three factors were associated with functional remission: shorter duration of prodrome ($OR = 0.50$, $p = .043$), severity of psychopathology (CGI-S, $OR = 0.51$, $p = .024$), and vocational status at service entry ($OR = 4.29$, $p = .003$).

Conclusions: While various aspects of pre-morbid functioning seem to correlate with the possibility of a favourable outcome in FEP patients who refuse medication, various limitations need to be taken into account in this study.

Talk 2

A Randomized Placebo Controlled Trial of Intensive Psychosocial Treatment Plus or Minus Anti-psychotic Medication for First Episode Psychosis With Low-risk of Self-harm or Aggression. The STAGES Study: Staged Treatment and Acceptability Guidelines in Early Psychosis

Shona Francey

Orygen, The National Centre of Excellence in Youth Mental Health, Melbourne, Australia

Background: Ethical early intervention in psychosis requires careful consideration of the risk:benefit ratio of treatments recommendations, especially the role of interventions with significant unpleasant side-effects. The STAGES Study aims to investigate whether intensive psychosocial treatment and close monitoring in a specialised early psychosis service, without antipsychotic medication, constitutes an effective treatment for a selected sub-group of young people with FEP.

Methodology: Young people entering the Early Psychosis Prevention and Intervention Centre (EPPIC) in Melbourne are screened for study eligibility and are invited to participate if they meet stringent inclusion criteria indicating low-risk of harm to self or others, and adequate social support. Participants are randomly assigned to receive either low dose antipsychotic medication or placebo for six months, and all participants receive intensive psychosocial treatment in the form of cognitive behavioural case management. Assessments of

psychopathology and neurocognitive performance, and neuroimaging occurs regularly until two years after study entry. Clinicians, participants and research staff remain blind to treatment allocation until the conclusion of the study.

Results: The study is ongoing with recruitment scheduled to conclude late in 2016. Over 70 young people (mean age 18.6 years, 45% male) with a range of psychotic disorder diagnoses have entered the study to date, demonstrating that the study is feasible and acceptable. This presentation will outline the study design and the baseline characteristics of participants.

Conclusion: This challenging study promises to contribute rich data about the impact of various treatments offered for first episode psychosis, and to further knowledge about factors affecting recovery.

Talk 3

THE STAGES Study: Medical and Safety Issues in Conducting a Trial That Involves the Management of Early Psychosis Without the Use of Antipsychotic Medication

Brian O'Donoghue^{1,2}

¹Orygen, The National Centre of Excellence in Youth Mental Health, Melbourne, Australia, ²Centre for Youth Mental Health, University of Melbourne, Australia

Background: The STAGES study is an RCT that involves the management of early psychosis with intensive psychosocial interventions and participants are randomised to receive either antipsychotic medication or placebo. Participants must meet stringent inclusion criteria, such as low risk of aggression or suicide. Additionally, the study protocol specifies strict discontinuation criteria in which the study medication is stopped (participants can continue to receive the intensive psychosocial interventions and are followed up as per protocol). This presentation will outline the safety issues involved in conducting this trial.

Methodology: The STAGES study is currently being conducted at the EPPIC clinic at Orygen Youth Health. The study protocol specifies the following circumstances in which the study medication must be discontinued: 1. an increase in suicidality 2. increase in aggression 3. significant increase in the severity of positive psychotic symptoms 4. significant decrease in functioning 5. request of participant 6. pregnancy. Criteria 1–3 are determined by the Brief Psychiatric Rating Scale.

Results: By May 2016, 77 young people had consented to participate in the STAGES study and 54.5% of participants were required to have their study medication discontinued. Reasons for discontinuation were: 24% ($N = 10$) increased risk, 19% ($N = 8$) insufficient improvement in psychotic symptoms, 19% ($N = 8$) participant request and 14% ($N = 6$) worsening symptoms. 7% ($N = 3$) were discontinued due to side-effects. Additionally, information on the required reporting of adverse events will be presented.

Conclusion: The STAGES study will provide valuable insights which will inform clinical guidelines, however strict safety measures are required for such a study.

Talk 4

Cognitive Therapy for People With a Diagnosis of Schizophrenia Spectrum Disorder Not Taking Antipsychotic Medication: A Single-blind Randomised Controlled Trial

Anthony Morrison

School of Psychological Sciences, University of Manchester, UK

Background: There is little evidence regarding whether psychological therapies can be effective as an alternative to antipsychotic medication. Our recent trial aimed to determine whether cognitive therapy (CT) is effective in reducing psychiatric symptoms experienced by people with schizophrenia spectrum disorders that have chosen not to take antipsychotic medication.

Methods: We conducted a two-site single-blind randomised controlled trial comparing CT plus treatment as usual (TAU) with TAU only. Participants were followed-up for a minimum of 9 and a maximum of 18 months.

Results: 74 participants with schizophrenia spectrum disorders who had chosen not to take antipsychotic medication psychosis (aged 16–65 years; mean 31.47; SD 12.27) were recruited. 37 were assigned to CT and 37 to TAU. Our primary outcome was the Positive and Negative Syndrome Scale (PANSS) total score. Changes in outcomes were analysed following the intention-to-treat principle, using random effects regression (a repeated-measures ANCOVA) adjusted for site, age, gender and baseline symptoms. Psychiatric symptoms were significantly reduced in the group assigned to CT in comparison with TAU, with an estimated between-group reduction in PANSS total of -6.52 (95% CI -10.79 to -2.25, $p = 0.003$).

Conclusions: CT significantly reduced psychiatric symptoms and appears safe and acceptable in people with schizophrenia spectrum disorders who have chosen not to take antipsychotic medication. Progress from an ongoing RCT evaluating CT in comparison to antipsychotic medication or a combination of both will also be described.

events, emotional reactivity, and psychotic experiences. In this symposium, we will present new data on the relationship between childhood adversity and psychiatric symptoms, and the relationship between childhood adversity and the subsequent onset of psychosis. We will then report on the extent to which cannabis use and urbanicity in UHR subjects are related to brain structure in this group. Experience sampling data will be presented, focusing on stress sensitivity in UHR subjects, and the extent to which this is associated with current psychopathology and clinical outcomes at follow up. Finally, we will report on the prevalence of autoantibodies to the NMDA receptor in high-risk subjects.

Talk 1

The Effect Of Environmental Risk Factors On Brain Structure In Those At Risk Of Developing Psychosis: Urbanicity And Early Cannabis Use

Matthew Kempton¹, Maria Calem¹, Stefania Tognin¹, Lucia Valmaggia¹, Philip McGuire¹, EU-GEI WP5 High Risk Study²

¹*Institute of Psychiatry, Psychology & Neuroscience, King's College London, UK*, ²*International Collaboration*

Abnormalities in brain structure have been confirmed in schizophrenia, and some of these abnormalities appear to be present before the onset of the illness. Currently it is not clear if these early brain abnormalities are associated with genetic or environmental risk factors. Urbanicity and early cannabis use are both recognized as important environmental risk factors for psychosis. In this study we examined the effects of these risk factors on cortical thickness in those at ultra high risk (UHR) of developing psychosis. UHR participants were recruited as part of the multicenter EU-GEI (European Union Gene-Environment Interaction) study and current and past cannabis use was assessed with the cannabis experience questionnaire (CEQ). We used the Social Environment Assessment Tool (SEAT) to examine participants' perceptions of their urban neighbourhood which included rating the built environment, crime and disorder, and neighbourhood co-operation. MRI data was acquired using the ADNI-2 sequence, and processed using the FreeSurfer. 230 structural MRI scans were acquired from participants with UHR at baseline. Data was available from 9 different cities around the world with wide variations in participant's scores of their urban environment. Seventy-four percent of UHR participants had previously used cannabis. The effects of urbanicity and cannabis use on cortical thickness are presented with a focus on brain regions known to be abnormal in UHR individuals. The findings discussed in this presentation may help in unravelling the mechanism of how exposure to particular environmental risk factors may contribute to the development of psychosis.

Symposium Session 3

Thursday, October 20

1:00–2:30 p.m. Manzoni

The EU-GEI High Risk Study: Adversity, Stress Sensitivity, Autoantibodies and Cortical Thickness

Chair: Philip McGuire, Co-Chair: Lucia Valmaggia

Speakers: Matthew Kempton, Tamar Kraan, Ulrich Reininghaus, Thomas Pollak

Institute of Psychiatry, Psychology & Neuroscience, King's College London, UK

A key rate-limiting factor in research on people at ultra high risk (UHR) for psychosis is that the samples in many studies are small, partly because it is difficult to recruit large numbers of subjects from a single centre. This issue can be addressed through multi-centre studies, and this symposium comprises the first presentation of findings from the EU-GEI High Risk Study. This study recruited $n = 369$ subjects at ultra high risk for psychosis from a network of 12 centres in Europe and Australia. A wide range of environmental factors that have previously been associated with psychosis were evaluated including, childhood adversity, substance use and the urban environment. MRI data were acquired on 3T scanners. Blood samples were collected for the analysis of CNS autoantibodies, and for genetic, epigenetic, metabolomic and proteomic analyses. Experience Sampling, a momentary assessment technique, was used to assess minor stressful

Talk 2

The Effect Of Childhood Abuse On 1-Year Outcome In Individuals At Ultra High Risk For Psychosis In The EU-GEI At Risk Study

Tamar Kraan¹, Eva Velthorst², Lucia Valmaggia³, Matthew Kempton³, Philip McGuire³, Filip Smit^{4,5,6}, Lieuwe de Haan¹, Mark van der Gaag^{7,8}, EU-GEI WP5 High Risk Study⁹

¹Academic Medical Center, University of Amsterdam, The Netherlands, ²Icahn School of Medicine, Mount Sinai, NY, US, ³Institute of Psychiatry, Psychology & Neuroscience, King's College London, UK, ⁴VU University and EMGO Institute for Health and Care Research, Amsterdam, The Netherlands, ⁵Trimbos Institute (Netherlands Institute of Mental Health and Addiction), Utrecht, the Netherlands, ⁶VU University Medical Center, Amsterdam, the Netherlands, ⁷Parnassia Psychiatric Institute, The Hague, The Netherlands, ⁸VU University, Amsterdam, The Netherlands, ⁹International Collaboration

Background: The association between childhood abuse and psychosis has been widely demonstrated in previous research. However, the effect of childhood abuse on transition to psychosis and other clinical and functional outcomes in individuals at ultra-high risk (UHR) for psychosis is not clear yet. The present study aimed to examine the effect of childhood abuse on transition to psychosis and other clinical and functional outcomes in UHR individuals of the EU-GEI study.

Methods: The sample consisted of 260 UHR subjects from the EU-GEI study with childhood trauma data and clinical and functional follow-up data available. Subjects were followed-up for two years. Clinical and functional outcomes were assessed at 6 months, 12 months and 24 months. Childhood trauma was assessed at baseline.

Results: Preliminary findings show that a history of childhood abuse was associated with an increased risk for transition to psychosis ($b = 1.36$, $p = 0.027$, CI 0.15 - 2.57). Moreover, a history of childhood abuse was associated with depression disorder ($b = 1.60$, $p < 0.001$, CI 0.76 - 2.44), post-traumatic stress disorder ($b = 6.18$, $p = 0.03$, CI 0.53 - 11.83), more severe anxiety symptoms ($b = .39$, $p = 0.033$, CI 0.03 - 0.74) and lower global functioning ($b = -4.20$, $p = 0.006$, CI -7.18 - 1.21) at follow-up.

Conclusion: A history of childhood abuse was associated with various clinical symptoms and poor global functional outcome, suggesting that childhood abuse is a pluripotent risk factor for psychopathology and poor global functioning in adolescence.

Talk 3

Stress Sensitivity As A Psychological Mechanism Underlying The Development Of Psychosis: Initial Evidence From The EU-GEI At Risk Experience Sampling Study

Ulrich Reininghaus¹, Barnaby Nelson², Eva Velthorst³, Matthew Kempton⁴, Lucia Valmaggia⁴, Philip McGuire⁴, Inez Myin-Germeys⁵, EU-GEI WP5 High Risk Study⁶

¹Maastricht University, The Netherlands, ²Orygen, The National Centre of Excellence in Youth Mental Health, Melbourne, Australia, ³Icahn School of Medicine at Mount Sinai, NY, USA, ⁴Institute of Psychiatry, Psychology & Neuroscience, King's College London, UK, ⁵KU Leuven, Belgium, ⁶International Collaboration

While contemporary models of psychosis have proposed a number of putative psychological mechanisms, how these contribute to the development of psychotic experiences in real life remains unclear. This study aimed to investigate whether elevated stress sensitivity, operationalized as stronger emotional reactions to minor stressors in daily life is an important psychological mechanism that contributes to the development of psychosis in help-seeking 'Ultra-High-Risk' (UHR) individuals. We used the Experience Sampling Method (ESM) to assess minor stressful events, emotional reactivity, and psychotic experiences occurring in the flow of everyday life in UHR individuals recruited from 3 sites (London, Amsterdam & The Hague,

Melbourne) and successfully completed ESM assessment with 80 UHR individuals. We found strong evidence of elevated stress sensitivity in UHR subjects, indexed by strong negative emotional reactions in response to event-related, activity-related, and social stress in daily life. Elevated stress sensitivity was, in turn, associated with increased odds of developing intense psychotic experiences in daily life. Event-related stress sensitivity was significantly elevated in UHR subjects with more severe symptoms and lower global functioning as measured with the GAF at 1-year follow-up. This is the largest multi-centre study using novel ecological momentary assessment technology conducted to date in UHR individuals. Our findings suggest elevated stress sensitivity may be an important psychological mechanism in the development of psychotic experiences in UHR individuals associated with more severe symptoms and lower global functioning.

Talk 4

Autoantibodies to the NMDA Receptor and Other Neuronal Cell-Surface Antigens in Subjects at Ultra-High Risk For Psychosis

Thomas Pollak¹, Matthew Kempton¹, Conrad Iyegbe¹, James Stone¹, Anthony David¹, Philip McGuire¹, EU-GEI WP5 High Risk Study²

¹Institute of Psychiatry, Psychology & Neuroscience, King's College London, UK, ²International Collaboration

Introduction: NMDAR autoantibodies have recently been identified in different cohorts of patients with psychotic disorders, with meta-analytical evidence indicating a higher prevalence in first episode psychosis. We sought to establish the prevalence and associations of autoantibodies to the NMDAR and other neuronal autoantigens in a group at ultra-high risk (UHR) for psychosis and their interaction with other markers of neuronal and blood-brain barrier (BBB) integrity.

Methods: Sera from 52 UHR subjects in the EU-GEI study and 11 healthy controls were tested using a fixed CBA: sera were incubated with HEK293 cells that had been transfected to express one of six autoantigens (NMDAR, AMPA-1, AMPA-2, CASPR2, LGI1, GABA-B); antibody binding was assessed using indirect immunofluorescence. Levels of S100B, a marker of BBB disruption, were assessed using a chemoluminescence assay.

Results: 15 out of 52 (28%) UHR subjects from the EU-GEI study vs 1 out of 11 (9%) control subjects had S100B values over the cutoff value of 0.10ug/L, suggesting potential discriminant utility in UHR. Data will be presented on the prevalence of neuronal autoantibodies and associations between baseline autoantibodies and S100B levels and transition to psychosis and functional outcome in UHR subjects.

Conclusions: Preliminary data suggests that a proportion of UHR subjects harbour potentially pathogenic autoantibodies and that S100B levels are raised in some UHR subjects, suggesting a disrupted BBB and/or concomitant neuronal/glial damage. Future work within the EU-GEI UHR cohort will assess the longitudinal course, clinical significance, MRI correlates and predictive utility of a panel of 30+ CNS autoimmune parameters.

Question and Answer Period

Discussant: Jim van Os, Maastricht University, The Netherlands

Symposium Session 4

Thursday, October 20

1:00–2:30 p.m. Foscolo

Putting Clinical High-Risk States and Staging Models to Work: Implications for Service Delivery

Chair: Jai Shah¹

Speakers: Jan Scott, Mary Cannon, Jai Shah, Ian Hickie
¹PEPP-Montréal, Department of Psychiatry, McGill University, Montréal, Canada

A key feature of contemporary staging models in youth mental health (YMH) is the “clinical high-risk” (CHR) or 1b stage, defined as one of sub-threshold symptoms or having a first-degree relative along with functional impairment. While these distressing syndromes require immediate care, the optimal setting and shape of clinical programming for CHR states is far from clear. At present, CHR services tend to be diagnosis-specific and affiliated with academic/tertiary care centres (most prominently in psychosis). However, the recent trend towards community-based, open-referral YMH systems has a myriad of implications, including the diagnosis and treatment of severe mental illnesses (SMI) in youth and the CHR states that precede them. This symposium considers these emerging issues in four countries currently undergoing YMH service transformations: Australia, Canada, Ireland and the UK. Presenters will discuss different models of expanding early intervention services to include CHR states, and their relative advantages and disadvantages. They will explain how recent studies have provided a novel validation of the CHR construct and its clinical utility for SMIs, generated important understandings of the relationship between attenuated symptoms and functioning in the CHR state, and identified optimal timing and multimodal opportunities for early intervention in stage 1b syndromes. Finally, they will explore how these findings inform the conceptualization, identification and treatment of CHR states. Since youth with CHR/stage 1b presentations make up approximately 50% of help-seekers to YMH services, these issues have tremendous relevance for the structure and orientation of YMH systems of care and their ongoing transformations.

Talk 1

What Next After EIP? An Overview of Possible Service Developments for the Early Stages of Severe Mental Disorders in the UK

Jan Scott

Institute of Neuroscience, Newcastle University, Newcastle upon Tyne, UK

Purpose: The UK has developed an extensive network of early intervention in psychosis (EIP) services over the last 15 years. However, discussions about future developments have led to the consideration of four potential ‘extension’ models: geographic extension; extension to all ‘at-risk’ youth; specialist service extension; and extension across all age groups with emerging psychosis.

Materials/Methods: This talk will describe these proposals, present the arguments used to support them, and examine the evidence for and against each model.

Results: Some EIP service providers argue that successful systems of care should not be changed, but that provision should be extended across the UK. In other localities, there is a desire to extend EIP services to encompass other clinical high risk groups and to move towards a trans-diagnostic youth mental health service. A third group of service providers have argued for specialist EI services for different diagnostic groups: this approach would support the development of services targeted at mood disorders (especially bipolar disorders),

leading to the provision of two parallel EI services. The fourth model argues that EIP should be limited to early stage psychosis, but without current any age limits, i.e. the service would accommodate 15 year olds alongside 50 year olds.

Conclusion: We conclude that the most logical extension model for EIP is for it to evolve into a trans-diagnostic youth mental health service, since the other proposed service models undermine one or more of the important principles that have made EIP such a successful strategy.

Talk 2

Prevalence of Prodromal Risk Syndromes Among “Non Help-Seeking” Adolescents in the Community: Influence of Assessment Criteria and Implications for Service Development

Mary Cannon, Ian Kelleher

Royal College of Surgeons, Dublin, Ireland

Purpose: There is relatively little knowledge about the prevalence of prodromal (CHR) syndromes in community settings. Thus far, research has been conducted only in the context of individuals attending “prodrome” services or clinics.

Methods: In order to address this issue, we assessed for psychotic symptoms, CHR risk syndromes and other psychopathology in 212 non help-seeking adolescents in schools.

Results: Between 1.5-8% of this community based sample fulfilled criteria for a CHR syndrome. The rate varied with the assessment criteria used, in particular the measurement of disability: without accounting for a global measure of functioning, the rate of prodromal syndromes was 8%; when poor functioning was included, the rate was 1.5%. Adolescents who met CHR criteria had a higher prevalence of other psychopathology, including a range of neuropsychological deficits compared with adolescents without psychotic symptoms and compared with adolescents who reported psychotic symptoms but who did not fulfil criteria for a prodromal risk syndrome.

Conclusions: Further research is greatly needed on prevalence, outcome and co-morbidity among “non help-seeking” individuals who fulfil criteria for prodromal risk syndromes in the community. The relatively high prevalence of CHR states in the non help-seeking general population has resource implications for setting up “at-risk” services in the community. Poor global functioning should be a key measure to be considered in such services, and the presence of psychotic symptoms alone should not necessarily indicate need for intervention.

Talk 3

Attenuated Psychotic Symptoms Prior to a First Episode of Psychosis: Retrospective Validation and Clinical Utility of the CHR Stage

Jai Shah^{1,2,3}, Anne Crawford^{1,2}, Sally Mustafa¹, Ridha Joobar^{1,2,3}, Ashok Malla^{1,2,3}

¹PEPP-Montréal, Douglas Mental Health University Institute, Montréal, Canada, ²McGill University, Montréal, Canada, ³ACCESS Open Minds, Montréal, Canada

Purpose: The relevance of staging models that incorporate CHR states rests partly on a key assumption that has gone untested: that the first episode of severe mental illness (SMI) is preceded by a CHR syndrome involving attenuated or sub-threshold symptoms. If few individuals presenting with a first episode SMI have experienced an earlier CHR state, then the clinical utility of potential interventions targeting CHR syndromes is significantly reduced.

Materials/Methods: In order to address this question, we used data from the Circumstances of Onset and Relapse Scale along with chart reviews and detailed interviews in a representative catchment area-based sample of 362 first episode psychosis (FEP) patients and their caregivers.

Results: From a list of 29 early signs and symptoms of psychiatric illness/distress, nine were identified by a group of expert psychologists and psychiatrists as reflecting attenuated psychotic symptoms during the prodromal period. A majority (238, 67.9%) of patients recalled experiencing at least one of these nine features, suggesting that the CHR state frequently precedes a FEP. At entry to FEP services, there were no differences in social, demographic, or clinical variables between those who had versus had not experienced attenuated signs/symptoms.

Conclusions: Most FEP patients experienced an earlier, identifiable CHR state, strengthening the latter's utility and relevance for early intervention (including prevention of SMIs). Intriguingly, early symptom profiles may fluctuate as the illness evolves and transitions into a full-blown SMI. These findings have significant implications for CHR states, transdiagnostic clinical staging models, and their effective operationalization in YMH services.

Talk 4

Implementation of Transdiagnostic Early Intervention Services for Anxiety, Mood and Psychotic Syndromes in Australia

Ian Hickie¹, Patrick McGorry^{2,3}, Shane Cross^{1,4}, Jane Burns⁵, Daniel Hermens¹, Elizabeth Scott¹

¹Brain and Mind Centre, University of Sydney, Australia, ²Orygen Youth Health Research Centre, Melbourne, Australia, ³Centre for Youth Mental Health, University of Melbourne, Parkville, Australia, ⁴School of Psychology, University of Sydney, Australia, ⁵Young and Well Cooperative Research Centre, Melbourne, Australia

Purpose: Over the last decade, Australia has implemented progressively primary-care based mental health assessment and psychological treatment services (headspace) that are open to persons aged 12-25 years with any form of psychological distress. Concurrent academic partnerships have developed a trans-diagnostic clinical staging model which differentiates early forms of illness with no or limited impairment (stages 1a and 1b) from established mood or psychotic disorders (stages 2+).

Materials/Methods: Extensive neuropsychological and neurobiological studies have identified correlates of these different stages of illness and compared the validity of staging models with more conventional, diagnosis-based systems.

Results: A range of studies indicate that clinical staging is more closely linked to neurobiological changes than to conventional diagnoses. We have implemented this model within specific service environments and studied the 12 month patterns of service use, changes in impairment and progression to later stages of illness.

Conclusions: The greatest opportunities for improving functional outcomes appear to be associated with the 3 month period following presentation for care. However, there is also a strong need to work more effectively over 12 months with those who are already impaired – independent of diagnoses. This work has major implications for further development of relevant mental health systems – favouring a more intensive 12 month program of clinical and psychosocial care, and tracking of outcomes for those with stage 1b anxiety, mood, psychotic or comorbid disorders. The capacity to deliver such programs of care may be taken to scale by smart use of adjunctive digital technologies.

Question and Answer Period

Discussant: Patrick McGorry, M.D., Ph.D., Orygen, the National Centre of Excellence in Youth Mental Health, Centre for Youth Mental Health, University of Melbourne, Parkville, Australia

Symposium Session 5 Thursday, October 20 2:45–4:15 p.m. Washington A

New Findings from the NIMH RAISE Early Treatment Program

Chair: John Kane¹, Co-Chair: Nina Schooler²

Speakers: John Kane, Delbert Robinson, Nina Schooler, Kim Mueser
¹Hofstra Northwell School of Medicine, New York, USA, ²SUNY Downstate, New York, USA

The RAISE-ETP clinical trial was funded by the National Institute of Mental Health and involved 404 first episode psychosis patients receiving care at 34 community mental health centres in 21 states across the U.S. Sites were cluster randomized to provide NAVIGATE, a manualized, comprehensive specialty care program including psychopharmacology, individual therapy, family psychoeducation/therapy and supported employment/education. We have previously reported on two year outcomes which indicated statistically significant advantages for the NAVIGATE intervention in quality of life, retention in care, psychopathology, and participation in work or school. Duration of untreated psychosis (with a median of 74 weeks) had a strong moderating impact on treatment effectiveness. This symposium will include unpublished data on: factors influencing rates of hospitalization, presented by John Kane; the role of supported education/employment in contributing to enhanced participation in work or school, presented by Kim Mueser; the impact of a computerized decision support system for prescribers designed specifically for this project, presented by Delbert Robinson; and an analyses of cognitive test measures as moderating and outcome measures, presented by Nina Schooler. Robert Heinssen will serve as discussant. This session will provide new data and further insights from the conduct of this study.

Talk 1

RAISE-ETP: Predictors of Hospitalization

John Kane^{1,2}

¹The Zucker Hillside Hospital, New York, USA, ²Hofstra Northwell School of Medicine, New York, USA

Purpose: The RAISE-ETP clinical trial was funded by the National Institute of Mental Health and involved 404 first episode psychosis patients receiving care at 34 community mental health centres in 21 states across the U.S. Sites were cluster randomized to provide NAVIGATE, a manualized, comprehensive specialty care program including psychopharmacology, individual therapy, family psychoeducation/therapy and supported employment/education. We have previously reported on two year outcomes which indicated statistically significant advantages for the NAVIGATE intervention in quality of life, retention in care, psychopathology, and participation in work or school. Duration of untreated psychosis (with a median of 74 weeks) had a strong moderating impact on treatment effectiveness. These analyses involved the hospitalization data in order to identify factors contributing to a higher risk of this outcome.

Materials and Methods: Multivariate analyses were conducted on the effect of baseline measures such as duration of untreated psychosis (DUP), number of prior hospitalizations, psychopathology and quality of life on time to hospitalization.

Results: The analyses revealed that participants with duration of untreated psychosis (DUP) of 74 weeks or longer were more likely than those with shorter DUP to be hospitalized (hazard ratio = 1.499), as were participants who had had more hospitalizations before study entry (hazard ratio 2.401). Higher baseline scores on the PANSS excited (hazard ratio = 1.089) and depressed (hazard ratio = 1.064) factors were associated with hospitalized.

Conclusions: These results underscore the potential importance of reducing DUP and successfully ameliorating symptoms such as excitement and depression.

Talk 2

Psychopharmacological Treatment in the RAISE-ETP Study: Outcomes of a Manual and Computer Decision Support System Based Intervention

Delbert Robinson^{1,2,3}

¹The Feinstein Institute for Medical Research, New York, USA, ²Hofstra Northwell School of Medicine, New York, USA, ³The Zucker Hillside Hospital, New York, USA

Purpose: RAISE-ETP compared NAVIGATE, a comprehensive treatment program for first episode psychosis (FEP), to clinician-choice Community Care (CC) treatment over a 2 year treatment period. Symptom and quality of life outcomes were better for NAVIGATE participants. Compared with prior comprehensive FEP interventions, NAVIGATE medication prescription included unique elements of 1) detailed specific first episode psychotropic medication guidelines and 2) a computerized decision support system to facilitate prescription decision making. We present comparisons of the psychotropic medications prescribed and the side effects participants experienced.

Methods: Prescription (medication name and daily dose) for all psychotropic medications were obtained using the Service Use and Resource Form administered monthly. At baseline, 3, 6, 12, 18 and 24 months, participants reported in a yes/no format whether they had experienced during the past 30 days any of 21 common side effects of antipsychotic medications.

Results: Over the 2 years, the 223 NAVIGATE participants compared to the 181 CC participants were more likely to be prescribed an antipsychotic (odds ratio: 3.734; 95% CI: 1.709, 8.162) and also an antipsychotic that conformed to NAVIGATE prescribing principles (odds ratio: 2.189; 95% CI: 1.084, 4.421). Despite an increased likelihood of antipsychotic prescription, NAVIGATE participants reported experiencing fewer side effects (treatment by time interaction, $F = 3.86$, $df = 5, 1143$, $p = 0.0018$). NAVIGATE participants were less likely to

be prescribed an antidepressant (odds ratio: 0.391; 95% CI: 0.162, 0.943).

Conclusion: As part of comprehensive care, medication prescription can be optimized for FEP, contributing to better symptom outcomes with less side effect burden than standard care.

Talk 3

Cognitive Functioning in First Episode Psychosis

Nina Schooler^{1,2}

¹The Zucker Hillside Hospital, New York, USA, ²SUNY Downstate Medical Center, New York, USA

Purpose: Significant cognitive impairment is already seen in first episode psychosis (FEP) and is recognized as an important moderator of long-term outcomes. An important question is whether specialized FEP treatment can improve cognitive functioning.

Materials and Methods: The RAISE-ETP study compared NAVIGATE, an integrated comprehensive treatment, to Community Care in 404 FEP patients at 34 sites in the US. Treatment continued for up to two years. The Brief Assessment of Cognition in Schizophrenia (BACS) was administered at baseline, one and two years. Age and sex adjusted T-scores for the BACS Composite and six sub-tests (Verbal Memory, Digit Sequencing, Verbal Fluency, Token Motor, Symbol Coding and Tower of London) were compared between treatments at each time-point.

Results: Compared to norms for all measures, this FEP sample (mean age 23; 75% male) performed at lower levels for Composite and sub-tests at baseline. The Composite Score was not significantly different between treatments at baseline, one or two years. The only individual test to show differences was Tower of London. Navigate participants had significantly better performance at baseline ($p = .04$) and at one-year ($p = .01$).

Conclusions: These results confirm findings of cognitive impairment in FEP psychosis. Further, comprehensive and intensive clinical treatment does not appreciably affect cognitive functioning. Presentation of these initial findings will be supplemented by consideration of moderators of cognitive measures, especially Tower of London which taps executive functions and problem solving. Moderation of clinical outcomes by cognition will also be presented. Addressing the cognitive dysfunction in FEP remains challenging.

Talk 4

Supported Education and Employment Outcomes in the RAISE-ETP Study

Kim Mueser

Boston University, Boston, Massachusetts, USA

Purpose: Increasing involvement in work and school are major objectives for first episode of psychosis (FEP) programs. However, the evidence for improvement in these outcomes has been mixed in comprehensive programs that do not include supported employment and education (SEE). Furthermore, research on FEP programs with SEE have focused on participants who want to work or return to school, limiting generalizability of findings to the broader FEP population. This analysis compared the effects of an FEP program with SEE on work, school, and public support outcomes to usual services.

Materials and Methods: FEP participants (N = 404) at 34 community clinics participated in a cluster randomized trial that compared usual Community Care (CC) to NAVIGATE, a comprehensive program with ≥5 hours/week per team of SEE. All NAVIGATE participants were offered SEE regardless of their interest in work or school. Monthly assessments over 24 months recorded days of employment, school attendance, and participation in SEE, and employment and public support income. General Estimation Equation models were used to compare CC and NAVIGATE on outcomes, and the mediating effect of receiving ≥3 SEE visits on outcomes.

Results: NAVIGATE was associated with a greater increase in work or school participation ($p = .0486$), which appeared to be mediated by participation in SEE. No differences were observed in work or school participation considered separately, or in earnings or receipt of public support payments.

Conclusions: The comprehensive NAVIGATE program for FEP approach improved involvement in work or school, and this effect appears to be mediated by participation in SEE.

Question and Answer Period

Discussant: Robert Heinssen, National Institute of Mental Health, Bethesda, Maryland, USA

Talk 1

Clinical Characteristics and Service use in Young People with Migration Background in an Early Intervention and Treatment Center

Andreas Bechdolf^{1,2,3,4}, Susanna Zarafonitis-Müller¹, Sonja Anouk Laier¹, Karolina Leopold¹

¹*Department of Psychiatry, Psychotherapy and Psychosomatics, Vivantes Klinikum am Urban, Early Intervention and Treatment Center – FRITZ am Urban, Charité Medical University, Berlin, Germany,*

²*Department of Psychiatry, Psychotherapy and Psychosomatics, Vivantes Klinikum im Friedrichshain, Charité Medical University, Berlin, Germany,* ³*Department of Psychiatry and Psychotherapy, University of Cologne, Cologne, Germany,* ⁴*ORYGEN, The National Centre of Excellence in Youth Mental Health, The University of Melbourne, Melbourne, Australia*

Purpose: Migration is as a crucial risk factor in psychoses, correlating with incidence, duration of untreated psychosis (DUP) and response to interventions. Access to early intervention services is an essential factor to improve the prognosis of young people with psychosis and migration background.

Methods: We evaluated service use and characteristics of patients with and without migration background who were treated in the early intervention and treatment centre (FRITZ) in Berlin, Germany. We compared characteristics of the FRITZ population with the characteristics of the catchment area.

Results: Compared to the characteristics of the catchment area the FRITZ sample presents a slightly lower proportion of people with migration background (35.6%) and a higher unemployment rate (45.8%). Regarding educational level 47.2% of our service users have university qualification, which corresponds to the characteristics of the catchment area. Migrants in the FRITZ showed significantly lower insight into illness than non-immigrants. FRITZ patients with migrant background were however better educated than non-immigrants of FRITZ and the average for migrants in the catchment area.

Conclusions: In terms of migration the characteristics of the FRITZ population corresponded to the characteristics of the catchment area. In this respect FRITZ seems to be well assessable. However, low educated people with migration background seemed to be underrepresented. We need more information about pathways to care and may need to rethink our awareness campaigns in order to improve engagement of people with lower education in our early intervention service.

Symposium Session 6

Thursday, October 20

2:45–4:15 p.m. Washington B

Migration and Ethnicity in First Episode Psychosis

Chair: Ingrid Melle¹, Co-Chair: James Kirkbride², Speakers: Andreas Bechdolf, Ilaria Tarricone, James B Kirkbride, Akiyah O Berg

¹*University of Oslo, Oslo University Hospital, Norway,* ²*UCL London, University of Cambridge, UK*

Migration background is recognized as a risk factor for developing psychosis. Ethnicity might influence symptom profiles and help-seeking behaviours. In Europe, having a migration- or ethnic minority background is partly overlapping since a large proportion of ethnic minorities also are first- or second generation immigrants. The current symposium includes studies from Germany, Italy, UK and Norway. It explores the role of migration background for the use of early intervention services, the risk of psychosis in internal versus external migrants thus exploring the role of ethnicity, the specificity of symptom dimensions across ethnic groups and finally investigation of factors that may mediate the associations between ethnicity and symptom profiles.

Talk 2

Increased Risk of Psychosis in Internal Migration: Results from the Bologna First Episode Psychosis Study

Ilaria Tarricone^{1,2,3}, Jane Boydell³, Arnisa Kokona¹, Frederico Triolo¹, Lisa Gamberini¹, Enrico Sutti¹, Michela Marchetta¹, Marco Menchetti^{1,2}, Marta DiForti³, Robin M Murray³, Craig Morgan³, Domenico Berardi^{1,2}

¹Bologna Transcultural Psychosomatic Team (BoTPT), Department of Medical and Surgical Sciences, University of Bologna, Italy, ²Department of Mental Health and Pathological Addictions, Bologna Local Health Trust, Bologna, Italy, ³Institute of Psychiatry, Psychology & Neuroscience, King's College London, UK

Purpose: Incidence of psychotic disorders is higher in many migrant groups; however, little is known about internal migrants (IM). This study aims to describe the incidence rates in natives to the region (NA), IM and external migrants (EM).

Method: All patients aged 18-64 years, with First Episode Psychosis (FEP), who made contact with the Bologna West psychiatric services, between 2002 and 2010, were included.

Results: 187 cases were included. Age and sex adjusted IR of psychosis per 100,000 per year were: 12.6 for NA, 25.3 for IM and 21.4 for EM. The IRR was 1.93 (1.19-3.13, $p = 0.007$) for IM and 1.79 (1.06-3.02, $p = 0.03$) for EM compared to NA.

Conclusion: Rates of psychosis were significantly elevated in IM as well as in EM. This result adds evidence as to the role of migration itself (versus ethnicity) on the risk of psychosis.

Talk 3

Do Symptom Dimensions Vary between Ethnic Groups at First Presentation to Early Intervention in Psychosis Services? Evidence from the SEPEA Study

James B Kirkbride^{1,2}, Chandni Hindocha³, Yasir Hameed⁴, Jesus Perez^{2,5}, Peter B Jones^{2,5}

¹Division of Psychiatry, UCL, London, UK, ²Department of Psychiatry, University of Cambridge, UK, ³Department of Clinical, Educational and Health Psychology, UCL, London, UK, ⁴Norfolk & Suffolk Foundation Trust, Ipswich, UK, ⁵Cambridgeshire & Peterborough NHS Foundation Trust, Cambridge, UK

Purpose: The risk of experiencing psychotic disorders is higher in several migrant and ethnic minority populations. We used data from a large cohort of people with first episode psychosis [FEP] to assess whether symptom dimensions at presentation to early intervention psychosis [EIP] services differ between these groups.

Method: Participants ($N = 683$, ages 16-35) with confirmed ICD-10 FEP (F10-33) were recruited from 6 EIP services over a 3.5 year period. Polychoric factor analysis identified 7 symptom dimensions (manic, depressive, disorganised, delusional, paranoid, thought disordered & hallucinatory symptoms). Linear regression analysis examined variation in symptom dimensions between 11 ethnic groups, first and later-generation migrants and age-at-migration, controlling for socio-demographic and clinical confounders.

Results: Symptom dimension between ethnic minority groups and white British participants were similar, and patterns did not differ between generations or age-at-migration. Compared to white-British participants people of black African origin experienced more manic ($\beta = 0.24$; 95%CI: 0.01, 0.47) and delusional ($\beta = 0.12$; 95%CI: 0.01, 0.23) symptoms, and less depressive symptoms ($\beta = -0.21$; 95%CI: -0.36, -0.06). People of Indian origin experienced more manic ($\beta = 0.81$; 95%CI: 0.05, 1.56), depressive ($\beta = 0.57$; 95%CI: 0.08, 1.06) and disorganised ($\beta = 0.43$; 95%CI: 0.03, 0.84) symptoms, but less delusional symptoms ($\beta = -0.41$; 95%CI: -0.78, -0.03).

Conclusion: Most ethnic groups, regardless of generation status or age-at-migration, present to EIP services with similar symptomatic

profiles in their first episode of psychosis. Nonetheless, differing symptom profiles in people of black African and Indian origins may warrant more nuanced treatment responses, and could underlie the relative excesses and absences of psychotic disorders observed in these populations.

Talk 4 Psychotic Symptom Profiles in Immigrants and Ethnic Minorities

Akiah O Berg, Mari Nerhus, Monica Aas, Ingrid Melle

NORMENT, K.G. Jebsen Centre for Psychosis Research, Division of Mental Health and Addiction, Institute of Clinical Medicine, University of Oslo, and Oslo University Hospital, Oslo, Norway

Purpose: Immigrants have heightened risks of psychotic disorders, and it is proposed that migration experiences influence symptom profiles. We have explored the following questions in patients with broadly defined psychotic disorders; 1. Do migration experience and/or ethnic minority status affect symptom profiles, and 2. Does experience of childhood trauma influence symptoms in patients from ethnic minorities, in particular auditory hallucinations?

Methods: Data for study 1 ($N = 1081/16.5\%$ ethnic minorities) and 2 ($N = 454/15\%$ ethnic minorities) were drawn from a large catchment area based sample of patients with broadly defined DSM-IV psychotic disorders. Current psychotic symptoms were measured with the Positive and Negative Syndrome Scale, lifetime verbal hallucinations during the SCID interview assessing and childhood trauma with the Childhood Trauma Questionnaire, self-report version.

Results: 1) Differences in symptom profiles between immigrants and Norwegians were primarily explained by socio-demographic factors such as age, education and diagnosis. Multivariate analyses indicated that ethnic minorities had more severe levels of delusions and difficulties in abstract thinking. 2) Patients from ethnic minority groups had experienced significantly more childhood traumas, had more current hallucinatory behaviour and lifetime experiences of auditory verbal hallucinations. Multivariate regression analyses showed that childhood trauma mediated the association between ethnic minority status and hallucinations.

Conclusion: Migration experiences and/or ethnic minority status do not directly influence psychotic symptom profiles. Higher symptom levels appear to be mediated by differences in socio-demographic factors and childhood trauma experiences.

Question and Answer Period

Discussant: Peter B. Jones, University of Cambridge, Cambridge, UK

Symposium Session 7

Thursday, October 20

2:45–4:15 p.m. Manzoni

Engaging Families in Early Psychosis Care Using CBT for Psychosis Informed Treatment

Chair: Kate Hardy¹

Speakers: Shirley Glynn, Kate Hardy, Yulia Landa, Juliana Onwumere

¹Stanford University, Palo Alto, CA, US

Families are integral to the care individuals with psychosis receive. They are often the first line of support for the individual and yet they are frequently excluded from treatment and experience care giver burnout and fatigue resulting in an impact on their own mental health. This need has been recognized in the early psychosis field, where the young person is often still living in the family home, and family intervention and peer support is recommended as a core component of specialized early psychosis services. However, despite this families still have trouble accessing specialized treatment within this setting due in part to the lack of resources, staff trained in specialist family interventions, and staff perceptions of working with families. This symposium will present different models developed to engage families in Cognitive Behavioural Therapy for psychosis (CBTp) informed care. Each of these models draw upon CBT interventions with the aim of supporting families to develop skills for self-care and to support their loved ones. Data from these models will be presented along with a discussion regarding implementation to address difficulties in large scale dissemination and training. In addition, the symposium will provide research based recommendations to clinicians and service managers for the inclusion of families in treatment in terms of supporting their loved one and managing their own mental health to reduce care giver burn out and ensure optimum engagement and treatment response for the young person.

Talk 1

The Role of Family Intervention in the RAISE Early Treatment Program

Shirley Glynn¹, Susan Gingerich², Kim Mueser³, Cori Cather⁴, John Kane⁵

¹UCLA Semel Institute for Neuroscience and Brain Behavior, Los Angeles, USA, ²RAISE NAVIGATE Training Coordinator, USA, ³Center for Psychiatric Rehabilitation, Boston University, USA, ⁴Massachusetts General Hospital and Harvard Medical School, USA, ⁵Division of Psychiatry Research, Zucker Hillside Hospital, North Shore–Long Island Jewish Health System, USA

Purpose: The Recovery After an Initial Schizophrenia Episode Early Treatment Project (RAISE-ETP) is a large multi-site US trial evaluating the benefits of coordinated specialty care on first psychotic episode. A key RAISE –ETP component is a comprehensive family intervention. This presentation will provide an overview, rationale, and engagement data pertaining to the RAISE-ETP family intervention.

Materials and Methods: Four hundred and four participants were randomized to RAISE-ETP or customary care; consenting to family participation in care was not an eligibility criteria. All RAISE-ETP participants were offered an individual family program. Much of the content mirrored the individual resiliency training, which included elements of cognitive-behavioural therapy for psychosis, and was offered to all consumers in RAISE-ETP.

Results: Seventy seven percent of the RAISE-ETP consumers were living with a relative; 68% had relatives who had at least one contact with the RAISE-ETP team and 52% attended at least one educational session. There was a mean (SD) of 6.39 (6.39) education sessions attended by relatives who had any contact with treatment team.

Mothers were the primary involved relatives, and consumers were present for 61% of the contacts. We are conducting further analyses to identify predictors and benefits of family engagement in RAISE-ETP.

Conclusion: Family engagement was achievable but challenging. Particular obstacles to engagement included divorced and blended families of origin, relatives who used illicit substances with the consumer, relatives who were hostile towards antipsychotic medication or mental health care, and role strain and distress in partners of individuals experiencing an initial psychotic episode.

Talk 2

Can Families Benefit from Learning CBT for Psychosis Skills?

Kate Hardy¹, Lizette Aguirre-Giron²

¹INSPIRE Clinic, Stanford University, Palo Alto, California, USA, ²Palo Alto University, California, USA

Purpose: Families are often the first line of support for young people experiencing a recent onset of psychosis. Despite this families are frequently excluded from treatment resulting in decreased access to important skills needed to support their loved one and address their own mental health needs as they help their family member navigate mental health services.

Methods: This study evaluates the impact of training family members in key Cognitive Behavioural Therapy for psychosis techniques over the course of a 2 ½ day workshop. In line with a cognitive-behavioural approach, the workshop aimed to help caregivers recognize specific stressors and the impact this has on their thoughts, emotions, and behaviours with a focus on developing appropriate coping strategies to support their own mental well-being. In addition, caregivers learned about the importance of developing collaborative relationships with their loved one through learning curious questioning techniques, acknowledging and addressing their own assumptions about symptoms, and applying coping skills to benefit the whole family.

Results: A total of 46 caregivers participated in the workshop. 65% were supporting someone within the family home while the other 35% were in contact with their loved one more than 15 hours per week. Participants reported high levels of satisfaction with the workshop.

Conclusion: This study demonstrated the feasibility of training caregivers in key CBT skills to address their own mental health needs and to support their loved ones. The talk will present quantitative and qualitative outcomes from this study and provide recommendations for training families in these skills.

Talk 3

Adaptation of CBT for Psychosis Training for Family Caregivers of Youth at Risk for Psychosis

Yulia Landa^{1,2,3}, Kim Mueser⁴, Michael Jacobs¹, Rachel Jespersen^{1,2,3}, Katarzyna Wyka^{3,5}

¹Icahn School of Medicine at Mount Sinai, NY, USA, ²Mental Illness Research, Education, and Clinical Center (MIRECC VISN 3), James J. Peter Veterans Affairs Medical Center, Bronx, New York, USA, ³Weill Medical College of Cornell University, New York, USA, ⁴Boston University, Massachusetts, USA, ⁵CUNY School of Public Health, New York, USA

Purpose: Teaching family caregivers CBT skills may serve as a protective factor for youth at-risk for psychosis, as it can help create a more supportive family environment, and sustain therapeutic gains made in time-limited CBT. We designed a comprehensive 15-week Group-and-Family-based Cognitive Behavioural Therapy Program (GF-CBT) that aims to facilitate functional recovery, decrease symptoms, and prevent transition to psychosis in youth at-risk. To teach family members how to apply CBT skills with their offspring, we adapted CBT for psychosis clinician training program, and augmented it with simulated learning (CBT skills are described, demonstrated, and role-played with a standardized patient actor).

Materials and Methods: Six families participated in an open feasibility trial, and 24 participate in a randomized controlled trial of GF-CBT. Simulation scenarios and the Cognitive Behavioural Therapy Skills for Families Scale (CBTSF-S) were developed to measure family members' proficiency at using CBT skills when communicating with youth displaying attenuated psychotic symptoms. Qualitative interviews about families' experience with the program were conducted.

Results: There were significant improvements in family members' communication and use of CBT skills at post-treatment. Family caregivers also reported increased understanding of their offspring's experiences, and greater confidence in their ability to help. Family members' empathy, as perceived by youth, also increased, and youth reported increased willingness to share with them distressing emotional experiences. Gains were largely maintained at the three-month follow-up.

Conclusion: Teaching CBT skills to family caregivers of youth at-risk for psychosis is feasible, and can benefit young individuals prone to psychosis and their families.

Talk 4

CBT for Psychosis: Can Informal Carers Play a Role?

Juliana Onwumere¹, Rosanna Michalczuk², Stephanie Learmonth¹, Elizabeth Kuipers^{1,3}

¹Institute of Psychiatry, Psychology & Neuroscience, King's College London, UK, ²Royal Holloway University, London, UK, ³Biomedical Research Centre, South London and Maudsley NHS Foundation Trust, London, UK

Purpose: Many individuals with psychosis, particularly during the first episode, will live with or maintain close contact with relatives (i.e. informal carers). There is a large body of evidence confirming the key role played by carers in supporting the recovery and wellbeing of relatives with psychosis, and facilitating their timely access to relevant services and care. Cognitive Behavioural Therapy for psychosis (CBTp) is an evidence based psychological talking therapy included in treatment guidelines across Europe and the USA. However, despite the independent contributions of CBTp and carer support to optimising patient outcomes, little is known about carer involvement in individual CBTp interventions.

Materials and methods: The current study employed focus group methodology to explore the views of 22 psychological therapists, working in early intervention and long-term psychosis populations, about including carers in CBTp interventions.

Results: Thematic analyses of interview data identified six distinct key themes comprising therapists' positive and negative experiences

of including carers in interventions; confusion about what therapy model was being used when carers were included in interventions; support needed for therapists who included carers in sessions, and flexibility around the timing of when to include carers.

Conclusion: Carers may have an important role to play in therapy. The talk will provide an overview of the key themes and review treatment and research implications.

Symposium Session 8

Thursday, October 20

2:45–4:15 p.m. Foscolo

Gender Differences in Emerging Psychosis

Chair: Anita Riecher-Roessler¹, Co-Chair: Anna Meneghelli²

Speakers: Anna Meneghelli, Anita Riecher-Rössler, Inez Myin-Germeys, Paolo Brambilla

¹Psychiatric University Clinics Basel, Switzerland, ²Ospedale Niguarda Ca' Granda Milan, Italy

Sex differences in schizophrenic psychosis have often been described, especially regarding the age of onset and the course of the disease. Little is known, however, regarding sex differences in emerging psychosis, i.e. the prodromal phase of psychosis and its first episode. In this symposium, we present data on sex differences from different studies and centres, regarding age at onset, duration of untreated illness, psychopathology, level of functioning, neurocognition, as well as stress reactivity, psychoendocrinology and neuroimaging. We will show how sexual dimorphism impacts on brain maturation trajectory from adolescence to adulthood. We will also show that there are not many significant differences between men and women regarding psychopathology and neurocognition, and if there are any, they seem to reflect general rather than patient-specific differences between men and women. On the other hand, stress reactivity seems to show distinct gender differences. The findings presented can shed some new light on the pathogenetic mechanisms of emerging psychosis.

Talk 1

Sex Differences in People at Ultra High-Risk of Psychosis

Anna Meneghelli¹, Antonio Preti²

¹*Ospedale Niguarda Ca'Granda, Milan, Italy*, ²*University of Cagliari, Sardinia, Italy*

Aims: Sex-related differences in the clinical expression and outcome of schizophrenia have long been recognized. This study set out to evaluate whether sex-related differences known to occur in the clinical expression and outcome of schizophrenia extend to those subjects who are judged at high risk of developing psychosis.

Methods: Detailed assessment of 140 patients with first-episode psychosis (FEP) and 120 subjects at ultra-high risk of psychosis (UHR) as enrolled at an early intervention program in northern Italy. All consecutive admissions were enrolled in the study. Standard criteria were used for diagnosis. Patients were assessed on validated scales aimed at measuring level of psychopathology and functioning.

Results: In both the FEP and the UHR samples, males outnumbered females. In FEP patients, women had been referred at an older age than men and had a shorter duration of untreated illness (DUI) and of untreated psychosis. In UHR patients, no sex differences were found in age of onset or DUI, nor statistically significant differences by sex were found in exposure to traumatic event, suicide attempt before enrolment, substance abuse. There was no diagnosis by sex interaction on symptoms severity or level of functioning at presentation.

Conclusion: The factors that are related to sex differences in age of onset of schizophrenia are specific to the full-blown psychosis and are less evident in the prodromal phases. Precipitating factors, such as stress and substance use and abuse might contribute to explaining sex differences in onset of schizophrenia, and may affect course and outcome as well.

Talk 2

Sex Differences in the At Risk Mental State and First Episode Psychosis

Anita Riecher-Rössler

University of Basel Psychiatric Clinics, Basel, Switzerland

Aims: To analyze sex differences in emerging psychosis, i.e. the prodromal phase of psychosis and its first episode.

Methods: We examined all patients referred to the specialized Early Detection Clinic of the University Psychiatric Hospital Basel and followed them up over at least 5 years regarding later transition to psychosis within the Basel FePsy (Früherkennung von Psychosen) study.

Results: We could so far analyze data of 173 at-risk mental state (ARMS) and 130 first episode psychosis (FEP) patients. As regards psychopathology, we did not find any significant gender differences. Regarding neurocognition, women performed better in verbal learning and memory independent of the diagnostic group. Men showed a shorter reaction time during the working memory task. In the subgroup of antipsychotic-naïve patients we found hyperprolactinaemia in a substantial proportion of FEP and ARMS, mainly in women. Pituitary volumes were increased in emerging psychosis (FEP and ARMS patients with later transition to psychosis > ARMS patients without later transition and healthy controls) and considerably larger in women than in men.

Conclusions: There do not seem to exist profound sex differences in symptomatology in the very early stages of psychosis. Sex differences in neurocognition seem to be similar to those in the healthy general population. Prolactin levels and pituitary volumes were increased in both genders, but much more in women than in men. These latter findings might indicate that emerging psychosis is associated with more stress for women than for men.

Talk 3

Sex Differences in Emotional Reactivity to Daily Life Stress in Emerging Psychosis

Inez Myin-Germeys

KU Leuven, Leuven, Belgium

Although it has long been suggested that men and women differ in their vulnerability to and expression of psychosis, recent studies did not find clear-cut sex differences. The current study examined self-reported psychotic experiences in context in order to more fully understand the extent and nature of sex differences along the psychosis continuity. 283 healthy controls, 268 subjects at genetic or psychometric risk for psychosis, and 232 patients diagnosed with a psychotic disorder were examined with ESM to investigate in the realm of daily life a) symptoms, b) behaviour in context, and c) underlying mechanism of stress and reward sensitivity. Multilevel regression analyses revealed very little differences in symptom expression and real life behaviour between men and women in daily life. Men and women did not differ in their level of social interaction and overall activity. However, men at increased risk of psychosis were more often alone and were less involved in goal-directed activities compared to women. Women reported more emotional reactivity to daily life stress than men but women also reported a higher increase in positive affect related to pleasant events. The data suggest only minor differences between men and women in psychotic symptoms and behaviour. Furthermore, they seem to reflect general rather than patient specific differences between men and women. The higher levels of stress-reactivity and reward-sensitivity in women compared to men point towards a protective factor, suggesting that increased environmental reactivity in women in addition to more social contacts may prevent the development of more severe psychopathology.

Talk 4

Sexual Dimorphism and Heterochronicity of Brain Maturation Trajectory From Adolescence to Adulthood

Paolo Brambilla

Ospedale Maggiore, Milan, Italy

Human brain maturation trajectory involves highly coordinated and sequenced events, but the impact of sexual dimorphism during the post-adolescence period has not been fully explored. The focus of the present study is to investigate sexual dimorphism in the post-adolescent phase of middle-age. A large European multi-site (EnPACT) sample of males and females between the ages of 18 and 60 was scanned to obtain 3D T1-weighted images, including healthy individuals and patients with major psychoses. Sampling density across the age-range was high. Step-wise changes during the developmental period were analyzed across subjects (separately by gender) using voxel-wise approaches. Changes in white matter and gray matter will be shown in both healthy and psychotic subjects. Our findings will help to clarify how the sexual dimorphism impacts on brain maturation trajectory from adolescence to adulthood and, consequently, the cognitive differences that have been documented between males and females, such as spatial abilities or verbal skills. Future studies should also consider the hormonal effects on brain maturation and possibly on behaviour in respect to sexual dimorphism.

Question and Answer Period

Discussant: Alison Yung, *Institute of Brain, Behavior and Mental Health, University of Manchester, UK*

Symposium Session 9

Thursday, October 20

4:30–6:00 p.m. Washington A

Pathways to Psychosis: New Evidence on Childhood Adversity and Social Stress Sensitivity in Early Psychosis

Chair: Mark van der Gaag¹, Co-Chair: Ulrich Reininghaus²

Speakers: Wim Veling, Jacqueline Counotte, Lucia Valmaggia, Ulrich Reininghaus

¹VU University, Department of Clinical Psychology, Amsterdam, The Netherlands, ²Maastricht University, Department of Psychiatry and Neuropsychology, Maastricht, The Netherlands

Evidence has accumulated that implicates various types of childhood adversity in the aetiology of psychosis. Although we know there is an association between childhood adversity and psychosis, we know very little about the putative mechanisms involved. Contemporary models of psychosis suggest that exposure to childhood trauma makes individuals more sensitive to subsequent social stress and, thereby, contributes to risk. This symposium brings together international researchers at the forefront of research into the role of social stress sensitivity as an important mechanism underlying the association between childhood adversity and psychosis using novel ecological momentary assessment (EMA) and virtual reality (VR) technology. Wim Veling will report new findings from an experimental VR study that heightened social stress sensitivity in virtual social risk environments mediates associations between childhood trauma, affective symptoms, and psychosis liability. Jacqueline Counotte will present novel data on the autonomic stress response to social stress using the same experimental VR design; decreased parasympathetic activity in virtual social risk environments was found in individuals with high psychosis liability. Lucia Valmaggia will report recent findings on the association between bullying-victimisation in childhood, heightened interpersonal sensitivity and paranoid ideation in individuals at ultra-high risk (UHR) for psychosis. Ulrich Reininghaus will present novel findings from an EMA study in first-episode psychosis patients, UHR individuals, and healthy controls that suggest social stress sensitivity is a risk and resilience mechanism underlying the association between childhood sexual abuse and psychosis. Peter Jones will discuss these findings in the context of new challenges and directions for future research.

Talk 1

Childhood Trauma and Social Stress Reactivity in Psychosis: A Virtual Reality Study

Wim Veling^{1,2,3}, Jacqueline Counotte², Roos Pot-Kolder^{2,4}, Jim van Os^{3,5}, Mark van der Gaag^{2,4}

¹University of Groningen, University Medical Center Groningen, Department of Psychiatry, Groningen, The Netherlands, ²Parnassia Psychiatric Institute, The Hague, The Netherlands, ³Maastricht University, Department of Psychiatry and Neuropsychology, Maastricht, The Netherlands, ⁴VU University, Department of Clinical Psychology, Amsterdam, The Netherlands, ⁵King's College London, King's Health Partners, Department of Psychosis Studies, Institute of Psychiatry, London, UK

Introduction: Childhood trauma may be related to risk for psychosis by the mechanism of sensitization to social stress. Virtual Reality (VR) provides the opportunity to test this mechanism by controlled experimental exposure to different social environments.

Methods: Fifty-five patients with recent onset psychotic disorder (FEP), 20 patients at ultra-high risk for psychosis (UHR), 42 siblings of patients with psychosis and 53 controls walked five times in a virtual

bar with different levels of environmental social stress. Virtual social stressors were population density, ethnic density and hostility. Social stress sensitivity was measured with paranoia and subjective distress in response to virtual social stress exposures, childhood trauma and self-esteem were assessed at baseline. Multilevel random intercept regression analyses were used to test childhood trauma as predictor and moderator of paranoia and subjective distress in VR. Social stress sensitivity was tested as mediator between childhood trauma and symptoms of psychosis.

Results: Childhood trauma was significantly associated with higher paranoia and subjective distress in the virtual social stress experiments. There was a positive and linear interaction between childhood trauma and degree of environmental social stress on paranoia and subjective distress. Social stress sensitivity measures mediated associations between childhood trauma, (minor) psychotic and affective symptoms, and psychosis liability.

Conclusions: Childhood trauma is associated with heightened social stress sensitivity and contributes to psychotic and affective dysregulation later in life by sensitized paranoid and stress response to social stressors.

Talk 2

High Psychosis Liability is Associated with Altered Autonomic Balance during Exposure to Virtual Reality Social Stressors

Jacqueline Counotte¹, Roos Pot-Kolder^{1,2}, Arie M. van Roon³, Olivier Hoskam⁴, Mark van der Gaag^{1,2}, Wim Veling^{1,3,5}

¹Parnassia Psychiatric Institute, The Hague, The Netherlands, ²VU University, Department of Clinical Psychology, Amsterdam, The Netherlands, ³University of Groningen, University Medical Center Groningen, Department of Psychiatry, Groningen, The Netherlands, ⁴GGZ Delfland, the Netherlands, ⁵Maastricht University, Department of Psychiatry and Neuropsychology, Maastricht, The Netherlands

Social stressors are associated with an increased risk of psychosis. Stress sensitisation is thought to be an underlying mechanism and may be reflected in an altered autonomic stress response. Using an experimental Virtual Reality (VR) design, the autonomic stress response to social stressors was examined in participants with different psychosis liability. Fifty-five recent onset psychosis patients, 20 patients at ultra-high risk for psychosis, 42 siblings of patients with psychosis and 53 controls were exposed to social stressors (crowdedness, ethnic minority status and hostility) in a VR environment. Heart rate variability parameters and skin conductance levels were measured at baseline and during VR experiments. High psychosis liability groups had significantly increased heart rate and decreased heart rate variability compared to low liability groups both at baseline and during VR experiments. Spectral analysis of heart rate variability showed that both low frequency (LF) and high frequency (HF) power were reduced and LF/HF ratio was unaltered compared to low liability groups, indicating decreased parasympathetic activity in patients with high psychosis liability. The number of virtual social stressors significantly affected heart rate, HF, LF/HF and skin conductance level in all liability groups. There was no interaction between psychosis liability and amount of virtual social stress. Thus, high liability to psychosis was associated with decreased parasympathetic activity in virtual social environments, which reflects generally high levels of arousal, rather than increased autonomic reactivity to social stressors. Our findings contribute to increased understanding of stress sensitisation and highlight the importance of cardiovascular risk management in psychosis.

Talk 3

Interpersonal Sensitivity and Bullying Victimization in those at Ultra High Risk of Psychosis

Lucia Valmaggia¹, J. McDonnell^{1,2}, Daniel Stahl¹, Paul Chadwick^{1,2}, Philip McGuire^{1,2}

¹King's College London, Institute of Psychiatry, Psychology and Neuroscience, London, UK, ²South London and Maudsley NHS Foundation Trust, London, UK

In this study we examined the potentially causal link between bullying-victimisation in childhood, heightened interpersonal sensitivity and paranoid ideation in the ultra-high risk group. Data were collected for 64 individuals in the ultra-high risk group for psychosis, and 43 healthy controls, using measures of interpersonal sensitivity, history of bullying, and state paranoid ideation in a virtual environment. Path analysis was conducted to explicate the relationship between these three variables of interest in the ultra-high risk group. The ultra-high risk group reported comparatively higher rates of historical bullying, interpersonal sensitivity and paranoid ideation. Path analysis indicated that interpersonal sensitivity fully explained the significant association between severe bullying in childhood and paranoid ideation in the ultra-high risk group. The significant role played by interpersonal sensitivity in the association between being bullied in school and paranoid ideation in the ultra-high risk group suggests that this should become a target for intervention.

Talk 4

Childhood Trauma, Social Stress Sensitivity and Psychosis: An Experience Sampling Study

Ulrich Reininghaus^{1,2}, Charlotte Gayer-Anderson², Lucia Valmaggia³, Matthew J. Kempton⁴, Helen L. Fisher⁵, Philip McGuire^{4,6}, Philippa Garety^{3,6}, Jim van Os^{1,4}, Robin M. Murray^{4,6}, Til Wykes^{3,6}, Inez Myin-Germeys⁷, Craig Morgan^{2,6}

¹Department of Psychiatry and Psychology, School for Mental Health and Neuroscience, Maastricht University, The Netherlands, ²Centre for Epidemiology and Public Health, Health Service and Population Research Department, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK, ³Psychology Department, Institute of Psychiatry, Psychology & Neuroscience, King's College, London, UK, ⁴Psychosis Studies Department, Institute of Psychiatry, Psychology & Neuroscience, King's College, London, UK, ⁵MRC Social, Genetic & Developmental Psychiatry Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK, ⁶National Institute for Health Research (NIHR) Mental Health Biomedical Research Centre (BRC) at South London and Maudsley NHS Foundation Trust and King's College London, ⁷Department of Medicine, Psychiatry Research Group, Catholic University of Leuven, Belgium

Evidence has accumulated that implicates childhood trauma in the aetiology of psychosis, but our understanding of the putative psychological processes and mechanisms through which childhood trauma impacts on individuals and contributes to the development of psychosis remains limited. We aimed to investigate whether stress sensitivity underlie the association between childhood abuse and psychosis. We used the Experience Sampling Method to measure stress, threat anticipation, negative affect, and psychotic experiences in 50 first-episode psychosis (FEP) patients, 44 At-Risk Mental State (ARMS) participants, and 52 controls. Childhood abuse was assessed using the Childhood Trauma Questionnaire. Associations of minor socio-environmental stress in daily life with negative affect and psychotic experiences were modified by sexual abuse and group (all $p < 0.05$). While there was strong evidence that these associations were greater in FEP exposed to high levels of sexual abuse, and some evidence in ARMS exposed, controls exposed were more resilient and reported less intense negative emotional reactions to socio-environmental stress. Elevated sensitivity and lack of resilience to socio-environmental stress in daily life may be an important

psychological mechanism underlying the association between childhood sexual abuse and psychosis.

Question and Answer Period

Discussant: Peter B. Jones, Department of Psychiatry, University of Cambridge, UK

Symposium Session 10

Thursday, October 20

4:30–6:00 p.m. Washington B

Striking Variation in First Episode Psychosis Across 15 Europe Sites

Chair: Robin Murray¹, Co-Chair: Jim Van Os²

Speakers: Craig Morgan, Marta Di Forti, Jim Van Os, Robin Murray
¹Institute of Psychiatry, Psychology & Neuroscience, Department of Psychosis Studies, King's College London, London, UK, ²University of Maastricht, Amsterdam, The Netherlands

Craig Morgan will show that incidence of psychosis across 15 sites in Europe, ranged from 10.0 per 100,000 in Cuenca, Spain to 63.9 per 100,000 in London, a six-fold difference. Incidence was highest in London (63.9 per 100,000) and Amsterdam (50.0 per 100,000) and lowest in northern European rural sites, and all southern European sites (e.g., Palermo, 12.8 per 100,000; Madrid, 21.6 per 100,000). Marta Di Forti will demonstrate that the lifetime prevalence of cannabis use across the 16 sites varied between 35% and 75% in cases, and between 24% and 60% in controls. London and Amsterdam had the highest proportion of daily users. The proportion of first episode psychosis cases attributable to cannabis (PAF) ranged from 6% to 25%, with London and Amsterdam having the highest PAF attributable to the use of high potency cannabis. Jim Van Os will show data concerning 'Jumping to Conclusions'. Working Memory, and psychotic symptoms from a general population sample ($n = 4597$). Alterations in JtC and working memory were associated with both psychotic and non-psychotic psychopathology. Cannabis use was associated with a more favourable cognitive profile, independent of psychopathology and demographic confounders. Robin Murray will consider predictors of treatment resistant schizophrenia (TRS) in two first episode psychosis studies; about one quarter of patients in each developed TRS. The majority were TRS from the onset, but a minority (20–30%) had originally responded to antipsychotics; the former may have a glutamatergic basis; the latter may result from antipsychotic-induced dopamine supersensitivity.

Talk 1**Similarities and Differences in Rates of Psychoses and Effects of Environmental Factors Across Europe**

Craig Morgan

Health Services and Population Studies, King's College, London, UK

As part of the EU-GEI programme, we completed a large multi-centre incidence and case-control study of psychotic disorders. In defined catchment areas in 15 sites in 6 countries, we identified a) all incident cases of psychotic disorder aged 18 - 64 years over 36 months and b) population-based samples of controls. We identified 2,553 cases from a total of 12,880,210 person years at risk. Crude incidence rates varied markedly from 10.0 per 100,000 person years in Cuenca, Spain to 63.9 per 100,000 in London, UK, a six-fold difference. Incidence rates were highest in northern European urban sites (e.g., London, UK 63.9 per 100,000; Amsterdam, Netherlands 50.0 per 100,000) and lowest in both northern European rural sites (e.g., Cambridge, UK 18.9 per 100,000) and all southern European sites (e.g., Palermo, Italy 12.8 per 100,000; Madrid, Spain 21.6 per 100,000). Our analyses to date have focused on childhood adversities (i.e., household poverty, household discord, neglect, bullying, and psychological, physical, and sexual abuse). The effects of these exposures were strikingly similar across sites. For example, the odds of physical abuse were between 1.5 and 3.5 times higher in cases compared with controls in all but one of the 15 sites. However, the prevalences of reported adversities in the control samples varied markedly among sites (e.g., physical abuse: 25.6% in London, UK; 6.3% in Oviedo, Spain). It may be that variations in incidence are, at least in part, a function of variations in the distribution of environmental risk factors across populations.

Talk 2**Geographical Differences in Cannabis Use Explain Variations in the Proportion of Cases of Psychosis Attributable to Cannabis Use Across Europe**

Marta Di Forti

Social Genetic and Developmental Psychiatry, Institute of Psychiatry, King's College, London, UK

Detailed data on pattern of cannabis use were collected from 1200 first episode psychosis patients and 1200 population controls across 15 sites from 6 European countries. DNA samples were also collected from all participants for GWAS analyses and to build a Schizophrenia-Polygenic Risk score (S-PRS). The measure of cannabis use that best predicted risk for psychosis consistently across sites was used in the interaction analyses with the S-PRS, expressed in quartiles, to investigate whether summary scores for Schizophrenia genetic load can explain variations in the risk of cannabis users to suffer from a psychotic disorder. Lifetime prevalence of cannabis use across the EU sites varied between 35% and 75% in cases and between 24% and 60% in controls. Age at first use was on average 16 years across the sites (SD 9.5). Frequency of use varied significantly across EU: London and Amsterdam had the highest proportion of daily users among cases and the highest availability of high potency type of cannabis. The proportion of cases attributable to cannabis use (PAF) varied between 6% and 25% with London and Amsterdam having the highest proportion of cases attributable to the use of high potency cannabis. Preliminary analyses of the S-PRS and data on frequency of cannabis use, using the entire sample ($n = 2400$), suggest a significant interaction between intermediate S-PRS quartiles and daily cannabis use on risk to suffer from psychosis. Thus, individual genetic load for schizophrenia, measured as PRS, significantly influences the probability of cannabis users to suffer a psychotic disorder.

Talk 3**Cognition, as a Transdiagnostic Factor Underlying Expression of Psychopathology, is an Important Phenotype for GxE Research**

Jim Van Os

Department of Psychiatry, University of Maastricht, Amsterdam, The Netherlands

We examined probabilistic reasoning bias, or 'Jumping to Conclusions' measured with the Beads Task (JtC) and a Working Memory task in a large general population sample ($n = 4597$), in order to analyse associations with psychotic and non-psychotic psychopathology, the impact of environmental factors on this phenotype, and possible gene-environment interactions, using polygenic risk scores. Psychotic symptoms were associated, adjusted for minority status and education, with both JtC and reduced working memory, particularly the combination of delusions and hallucinations and the combination of psychotic and non-psychotic symptoms. Cannabis use, independent of psychosis, was associated with BETTER working memory and LESS tendency to JtC, whereas childhood trauma was not associated with either. Results of GxE analyses will be presented. Associations between psychotic symptoms on the one hand, and JtC and working memory on the other were not specific, as similar associations existed with any mood disorder, even in those without psychotic symptoms. The results suggest that alterations in JtC and working memory are associated with both psychotic and non-psychotic psychopathology in the general population, independent of environmental risks. Cannabis use was associated with a more favourable cognitive profile, independent of psychopathology and demographic confounders.

Talk 4**Early and Late Types of Treatment Resistant Schizophrenia Develop in Patients with First Episode Psychosis Followed Up For 5-10 Years**

Robin Murray, Arsime Demjaha, Olesya Ajnakina

Psychosis Department, Institute of Psychiatry, King's College, London, UK

Surprisingly little is known about treatment resistant schizophrenia (TRS), its predictors, and the mechanisms which underlie it. We studied the development of TRS in two large first episode psychosis studies from the UK; the first, the AESOP study was followed-up for 10 years and the second, the GAP study for 5 years. The outlook for first episode psychosis as a whole was good with 62% of those in the AESOP study having no significant psychotic symptoms at ten years. However, about one quarter of patients in each sample (AESOP and GAP) developed TRS. Between 70 and 83% of TRS patients were non-responders from the onset of psychosis in the two studies, GAP and AESOP respectively, but a minority (17-30%) had originally responded to antipsychotics but then became TRS. Neurochemical imaging data suggest that the former group do not show any abnormality of striatal dopamine but rather show increased glutamate in the anterior cingulate; some tentative evidence (e.g. earlier onset, male gender, predominant negative symptoms) suggest that this group may have a neurodevelopmental origin. In contrast, the late onset TRS group may result from antipsychotic-induced dopamine supersensitivity; i.e. the compounding of the original presynaptic dopaminergic abnormality with an iatrogenic postsynaptic pathology.

Symposium Session 11

Thursday, October 20, 4:30–6:00 p.m., Manzoni

PEPPNET: A National Network to Support Coordinated Early Psychosis Service Development

Chair: Kate Hardy¹

Speakers: Steven Adelsheim, Vinod H. Srihari, Kate Hardy, Laurie Flynn

¹Stanford University, Palo Alto, California, USA

Early psychosis service implementation in the United States has lagged behind other countries. Centres of excellence for early psychosis research and treatment exist, typically affiliated with academic settings, but there is generally a dearth of treatment options within the community. However, recent federal initiatives allocated a 10% funding set aside from the Mental Health Block Grant (increased this year from 5%) specifically to target early psychosis service development. Additionally, the publication of outcomes from the RAISE initiative has heightened public interest in this issue and demonstrated the impact of providing these services within a community setting. This has resulted in increased demand from the public, and community agencies, for access to these types of services. The Prodromal and Early Psychosis Program Network (PEPPNET) was developed in 2014 bringing together national experts in early psychosis from across the United States. PEPPNET aims to address implementation challenges and requests from agencies and providers for guidance and technical assistance to support service development. The network consists of a steering committee and three workgroups with participants from academia, community agencies, federal agencies, and those with lived experience. This symposium will describe the unique structure of this network and the roles of each of the workgroups including outcomes from surveys and discussions generated in these workgroups. The symposium will be of interest to those interested in advocacy, implementation efforts at a national level, and broad dissemination of information to providers to support practice change.

Talk 1

Implementation of a National Early Psychosis Clinical Support Program in the United States: The Prodrome and Early Psychosis Program Network (PEPPNET)

Steven Adelsheim¹, Vicki Harrison¹, Robert Heinssen², Jane Isaacs Lowe³, Gary M. Blau⁴

¹Stanford University, Palo Alto, CA, USA, ²Division of Services and Intervention Research, National Institute of Mental Health, Bethesda, Maryland, USA, ³Robert Wood Johnson Foundation, Princeton, New Jersey, USA, ⁴Center for Mental Health Services, Substance Abuse and Mental Health Services Administration, Rockville, Maryland, USA

Purpose: The Prodrome and Early Psychosis Program Network (PEPPNET) provides technical assistance and clinical support for the growing number of clinical programs focused on supporting those with clinical high risk or early psychosis across the United States (US). **Materials and Methods:** Four core working groups have been developed to support PEPPNET member program site implementation, including the overarching steering group, which consists of convening members from research, clinical care, advocacy, lived experience, and federal/local agencies. In addition, the three subcommittees of training, treatment, and lived experience provide coordination and technical expertise in site implementation. Other core components of PEPPNET include registration of over 200 PEPPNET members from sites across the country, launch of a national list-serve, a newsletter and website.

Results: PEPPNET's infrastructure and workgroups provide critical coordination and support for the rapidly expanding number of clinical early psychosis sites across the US. With additional federal funding coming to each US state, the need to ensure evidence-based training and implementation continues to grow in both scope and urgency. In partnership with other founding agencies, PEPPNET is quickly moving to fill that gap.

Conclusion: While sustainable funding for PEPPNET remains a question for the future, the Network continues to provide valuable coordination of local program development and technical assistance.

Talk 2

PEPPNET Treatment Workgroup for Early Intervention Services (EIS)

Vinod H. Srihari^{1,2}, Lisa Dixon^{3,4}

¹Department of Psychiatry, Yale University School of Medicine, New Haven, CT, USA, ²Program for Specialized Treatment Early in Psychosis (STEP), New Haven, CT, USA, ³Columbia University Medical Center, New York, NY, USA, ⁴New York State Psychiatric Institute, New York, NY, USA

Purpose: Studies have tested a variety of multi-element packages for EIS, but substantial uncertainty remains regarding what specific treatment components are critical for different subgroups in different settings. In the US, "coordinated specialty care" has been offered as a starting point. However, new services can draw from a wealth of empirically based treatments and implementation experiences when designing packages of care.

Methods: This workgroup facilitates dialogue on candidate treatment components for individuals at clinical high risk for, or experiencing first episode psychosis. This is a rapidly evolving field, and one in which service context and population may impact choice of treatments and their effectiveness. Thus, rather than identify core components, emphasis is placed on sharing expertise in various empirically based approaches with adequate discussion of implementation context.

Results: A monthly tele-forum has elicited broad representation from programs across the country, and interest in a variety of treatments (e.g. CBTp, supported education). Brief presentations by content experts are followed by active discussions focused on adaptations and implementation challenges. Slide presentations, written summaries and recordings of all workgroup meetings have been made available online. The workgroup will include problems without defined treatments (e.g. disengagement) or for which program level responses are necessary (e.g. reducing duration of untreated psychosis). Benchmarks for relevant effectiveness outcomes will be considered, to support high standards of practice across these services.

Discussion: This model for sharing expertise can support implementation of new programs, and refinement of established services, all toward optimizing the public health impact of early intervention.

Talk 3

PEPPNET: Addressing Training and Technical Assistance Needs in the Community

Kate Hardy¹, Tamara Sale²

¹Stanford University, Palo Alto, CA, USA, ²Portland State University, Portland, OR, USA

Purpose: Increased understanding of the need for widespread early psychosis implementation in the United States has resulted in community agencies seeking appropriate consultation and training to support service development efforts. Unfortunately, despite dedicated federal funding, there is no national guidance to support these efforts. This has resulted in agencies reporting confusion as they research the different early psychosis models currently available in the United States in particular recognizing a need to adapt these models to fit their community but unsure as to how to do so.

Methods: The Training and Technical Assistance (TA) workgroup meets monthly as part of the Prodromal and Early Psychosis Program Network (PEPPNET) and was formed to address the training and TA needs of communities implementing early psychosis services, to share information about training and TA, and to build a national infrastructure to support effective implementation. It comprises of members from across the United States currently engaged in both the development and delivery of training and TA related to early psychosis implementation.

Results: A survey of PEPPNET members was conducted to assess training and TA needs and initiatives. Results indicated a three-tiered approach to training and TA and an overwhelming recognition that demand has surpassed supply. The group has also created consensus document to support new service development initiatives in the community.

Conclusions: The surge in early psychosis service development is welcomed however it has associated challenges with the provision of evidence-based training. The national Training and TA workgroup addresses these challenges to support widespread implementation.

Talk 4

PEPPNET: Integrating Peers and Individuals with Lived Experience into National Service Development and Reform

Laurie Flynn

NAMI NYC Board of Directors, New York, USA

Purpose: First episode psychosis is a profoundly distressing experience. The young person and their family are often frightened and bewildered. Effective early psychosis programs must begin where the person is, listening to their experience and needs. It's vital that programs engage, inform and support an ongoing partnership for recovery. The voice of individuals with lived experience (both consumers and families) is crucial to this process. PEPPNET leaders respect the voices of peers and family members and formed a workgroup of a diverse group of peers and caregivers involved in outreach, education and advocacy.

Method: Monthly teleconferences were formed to exchange information, discuss projects and work towards achieving the workgroup goals of: 1) Raising awareness and incorporate best practices in working with families and people with lived experience. 2) Helping engage and educate consumers/families on clinical aspects of care, 3) Helping engage, recruit and promote these programs.

Results: Active for nine months, we've already had an impact. Members of our workgroup joined the other PEPPNET workgroups (Training & Technical Assistance and Treatment) providing updates on our activities and concerns. We focused on two strategic projects: 1) adapting resources aimed at incorporating cultural awareness across early psychosis recruitment and treatment, 2) developing an online survey to collect experiences of peers and families in their initial contact with the mental health system.

Conclusion: The lived experience workgroup is using our collective knowledge to inform education and recruitment efforts, increase access to early psychosis programs, and advocate for mental health system reform.

Symposium Session 12

Thursday, October 20, 4:30–6:00 p.m., Foscolo

The Long Journey from Biological Markers, Environment Adversities and Treatment Effectiveness of Early Interventions on Psychosis - Data from the GET UP Project in Community Services Serving a 10 million Inhabitant Catchment Area

Chair: Mirella Ruggeri¹, Co-Chair: Maximilian Birchwood²

Speakers: Luisella Bocchio Chiavetto, Letizia Squarcina, Maximilian Birchwood, Juliana Onwumere

¹Section of Psychiatry, Department of Neuroscience, Biomedicine and Movement, University of Verona, Italy, ²Mental Health and Wellbeing, Warwick Medical School, Coventry, UK

In this Symposium, a set of data on biological and environmental markers and moderators of response in patients and their relatives to standard and innovative interventions in psychosis will be discussed. More specifically, we will present a body of evidence on Immune and Metabolic Alterations, cognitive and neuro-functional and neurological endophenotypes; cerebral morpho-functional and neuropsychological markers of prognostic value and on adverse events that can contribute to enhancing treatment response, patients' clinical improvement and relatives coping skills. Data from the research programme "Genetics Endophenotypes and Treatment: Understanding early Psychosis" (GET-UP) funded by the Italian Ministry of Health, which aims to apply innovative and targeted forms of intervention for first episode psychosis and to test its effectiveness and feasibility in the community care will be presented. The randomised controlled trial launched in the frame of the GET UP research Programme is based on sophisticated epidemiological, clinical, environmental biological, and neurocognitive investigations and involves 117 Mental Health Centres located throughout a 10 million-inhabitant catchment area, including two Regions (Veneto and Emilia Romagna) and the Bolzano, Florence, and Milan provinces. This is the largest Trial ever conducted so far in this field and aims to enhance knowledge of clinical, social, and environmental predictors for illness course, outcomes, and treatment response and providing key information to orient prognostic judgement, plan targeted and individualized intervention.

Talk 1

Molecular Markers of Psychosis Onset: Immune and Metabolic Alterations in First Episode Psychosis (FEP) Patients

Luisella Bocchio Chiavetto¹, Roberta Zanardini², Clarissa Ferrari², Sarah Tosato³, Antonio Lasalvia³, Paolo Santonastaso⁴, Giovanni de Girolamo², Francesca Pileggi⁵, Fausto Mazzi⁶, Emanuela Leuci⁷, Mirella Ruggeri², Massimo Gennarelli³

¹IRCCS Fatebenefratelli Brescia, Italy, ²University of Verona, Italy,

³University of Brescia, Italy, ⁴University of Padova, Italy, ⁵AUSL Bologna, Italy, ⁶AUSL Modena, Italy, ⁷AUSL Parma, Italy

Purpose: The molecular underpinnings associated to first episode psychosis (FEP) remains to be elucidated, but this issue is of great interest considering the usefulness of possible biomarkers for the improvement of diagnosis and treatment personalization. Compelling evidence supported an association of FEP with blood alterations in immune system, neurotrophins, growth factors and metabolism regulators.

Materials and Methods: In order to identify possible biomarkers for differential diagnosis in FEP patients, the serum levels of the neurotrophins BDNF and VEGF, the cytokines IL-1RA, IL-6, IL-10 and IL-17, RANTES, MIP-1 beta, IL-8 and the metabolic regulators C-peptide, Ghrelin, GIP, GLP-1, Glucagon, Insulin, Leptin, PAI-1, Resistin and Visfatin were analysed in 260 subjects collected in the GET-UP project (49 were controls).

Results: The results indicated alterations of serum VEGF, MIP-1, IL-6, Ghrelin, GLP-1, Glucagon and PAI-1 in FEP patients ($p < 0.01$). The principal component analysis (PCA) revealed that the most important variables to discriminate patients versus controls are Ghrelin, Glucagon, VEGF and MIP-1. Moreover, a significant increase of IL-8 serum levels in patients with an affective psychosis diagnosis vs other FEP patients was observed ($p = 0.008$). The ROC analysis evidenced a high discrimination performance of MIP-1 concentrations in classifying patients (AUC = 0.864), whereas only a weak effect was found for IL-8 measures in the identification of affective psychosis vs other FEP diagnoses (AUC = 0.629).

Conclusion: The data evidenced a dysregulation in the inflammatory system and glucose metabolism in FEP patients, in line with previous findings, nevertheless none of the studied markers showed a potential usefulness for the differential diagnosis.

Talk 2

Classification of First-Episode Psychosis Using Machine Learning Techniques on Multimodal Multisource MRI Data

Letizia Squarcina¹, Umberto Castellani¹, Marcella Bellani¹, Cinzia Perlini², Nicola Dusi¹, Mirella Ruggeri², Paolo Brambilla³

¹AouI Verona, Italy, ²University of Verona, Italy, ³University of Milano, Italy

First episode psychosis (FEP) patients are of particular interest for neuroimaging investigations because of the absence of confounding effects due to medications and chronicity. Nonetheless, imaging data are prone to heterogeneity because for example of age, gender or parameter setting differences. In our recent works, we tried to automatically discriminate FEP patients and normal controls on the basis of multi-modal magnetic resonance imaging (MRI) data. In particular we have employed support vector machine (SVM) classifiers on gray matter structures, white matter fibre bundles, and perfusion indexes. Brain hemodynamic and structural changes have been reported in major psychosis in respect to healthy controls, and could be therefore of relevance for the onset of psychosis. In general, our studies show that multivariate machine learning approaches integrating multimodal and multisource imaging data can classify FEP patients with high accuracy. Interestingly, specific grey matter structures and white matter bundles reach high classification reliability when using

different MRI modalities and indices, with particular regards to frontal and temporo-parietal areas. Therefore, we found evidence that brain perfusion, cortical thickness, and white matter integrity can be used as potential markers to classify patients with FEP.

Talk 3

From Childhood Adversity to First-Episode Psychosis: Associations Between Social Environment and Specific Symptom Profiles. Data from the GET UP PIANO Trial

Maximilian Birchwood¹, Rosa Ritunnano², Andrew Thompson¹, Rachel Upthegrove³, Katia De Santi⁴, Chiara Bonetto², Doriana Cristofalo², Angelo Fioritti⁵, Antonio Lasalvia⁴, Sarah Tosato², Mirella Ruggeri², The GET UP Group²

¹Mental Health and Wellbeing, Warwick Medical School, Coventry, UK,

²University of Verona, Italy, ³University of Birmingham, Edgbaston, West Midlands, UK, ⁴AOUI Verona, Italy, ⁵AUSL Bologna, Italy

Purpose: Childhood adversity increases risk of developing psychiatric symptoms including those belonging to the psychosis continuum, and predisposes to more negative outcomes. However, the pathways leading from early adverse experiences to outcome trajectories in first-episode psychosis (FEP) are yet to be revealed. We explored the associations between specific forms of childhood adversity and individual psychotic symptoms in a large, representative and well-characterized sample of FEP patients.

Methods: The study was conducted within the framework of the Psychosis early Intervention and Assessment of Needs and Outcome (PIANO) Trial - part of the larger research program "Genetics Endophenotypes and Treatment: Understanding early Psychosis" (GET UP). Symptom severity was evaluated using the Positive and Negative Syndrome Scale (PANSS). Information on childhood adversity was obtained from 356 patients (80.2%) using the Childhood Experience of Care and Abuse Questionnaire (CECA-Q).

Results: Maltreated FEP patients showed higher positive and affective symptoms, poorer premorbid adjustment and impaired global functioning. Physical abuse showed a significant association with grandiosity (OR 2.28), unusual thought content (OR 2.05), motor retardation (OR 2.12) and emotional withdrawal (OR 1.85). Sexual abuse was associated with guilt feelings (OR 2.10). Parental neglect was associated with passive-apathetic social withdrawal (OR 1.75) and active social avoidance (OR 1.82). Estimated ORs remained significant after adjusting for age, sex and lifetime cannabis use.

Conclusions: Different forms of childhood adversity may foster a specific and more severe

Talk 4

Identifying Moderators and Predictors of Treatment Outcome in Caregivers. Results from the GET UP PIANO Pragmatic Cluster Randomized Controlled Trial

Juliana Onwumere¹, Elisabeth Kuipers¹, Paul Bebbington², Chiara Bonetto³, Doriana Cristofalo², Carla Cremonese⁴, Maurizio Miceli⁵, Silvio Scarone⁶, Anna Meneghelli⁷, Giovanni de Girolamo⁸, Mirella Ruggeri³, The GET UP Group³

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Background: Over the last decade, family interventions (FI) and cognitive behavioural therapy (CBT) have featured in psychosis treatment guidelines in different countries and alongside case management, form part of optimal packages of care in first episode psychosis (FEP) services. Robust evidence in support of their efficacy and acceptability to clinical groups is well established. However, data remains scarce and our understanding limited, on moderators of treatment outcome for carers in FEP services. This study investigated what carer and patient demographics and clinical profiles were associated with gains from psychosocial treatment interventions within FEP services.

Methods: Data was collected as part of the GET UP (Genetics, Endophenotypes, Treatment: Understanding early Psychosis) PIANO (Psychosis: early intervention and Assessment of Needs and Outcome) pragmatic cluster RCT that compared additional psychosocial intervention (CBT, FI case management) with treatment as usual for FEP cases in 126 mental health centres in Italy. Patients were assessed with a range of clinical assessments before treatment initiation and 9 month follow up.

Results: Significant interactions were identified between psychosocial interventions, patient and carer factors and carer outcomes. The results suggested that psychosocial interventions, when compared to routine care alone, delivered greater reductions in carer distress particularly in patients reporting higher levels of carer EE and more negative accounts of early caregiving experiences and carers reporting greater caregiving hours. Further analyses are in progress.

Conclusions: Current findings are encouraging and offer indications for future investigations. Further studies are required to replicate the findings and assess the contribution of local contexts.

Symposium Session 13

Friday, October 21, 1:00–2:30 p.m., Washington A

Immunotherapies for Psychosis and Depression: Promising New Lead or a Blind Alley?

Chair: Peter B. Jones¹, Co-Chair: Merete Nordentoft²

Speakers: Valeria Mondelli, Golam Khandaker, Belinda Lennox, Michael Benros

¹University of Cambridge, Cambridge, UK, ²University of Copenhagen, Copenhagen, Denmark

Contrary to the traditional view that the brain is an immunologically privileged site shielded behind the blood-brain barrier, emerging evidence indicate complex interactions between the immune system and the brain that can lead to changes in mood, cognition and

behaviour. Convincing evidence from epidemiological, genetic, and experimental studies now implicate the immune system in the pathogenesis of major mental disorders such as schizophrenia and depression. Focusing on new clinical studies and meta-analysis of treatment trials, this symposium will provide an update on the relevance of inflammation and auto-immunity for treatment of psychosis and depression, and argue whether it is now time for evidence-based immunotherapeutic strategies to enter psychiatric clinics. Dr Mondelli (Institute of Psychiatry, Psychology and Neuroscience) will present evidence showing that activation of proinflammatory immune response, as reflected by elevated circulating inflammatory cytokine levels (e.g. IL-6, INF- γ), is associated with poor antipsychotic response in first episode psychosis. Dr Khandaker (University of Cambridge) will present data showing that inflammatory cytokines (e.g. IL-6) play a role in the development of psychotic and depressive symptoms, symptom persistence, followed by a meta-analysis of RCTs demonstrating effectiveness of anti-cytokine treatment for depression in people with chronic inflammatory illness. Dr Lennox (University of Oxford) will discuss the evidence for effectiveness of immunotherapies for psychotic disorders particularly patients with NMDAR auto-antibodies. Dr Benros (University of Copenhagen) will present novel findings regarding immunological risk factors for schizophrenia and depression from Danish population-based studies, followed by a meta-analysis of anti-inflammatory treatment for depression.

Talk 1

Inflammation and Response to Antipsychotic Treatment

Valeria Mondelli

Institute of Psychiatry, Psychology and Neuroscience, King's College London, Department of Psychological Medicine, London, UK

Background: Activation of the immune system has recently been reported in several studies in patients with first episode psychosis. However, the consequences of this increased inflammation remain still unclear. In this presentation I aim to show some of our recent studies investigating the effects of increased inflammation on clinical outcome and physical health in patients with first episode psychosis.

Methods: We collected blood samples in patients with first episode psychosis and healthy controls. To evaluate inflammation we assessed serum levels and blood mRNA levels of interleukin-6 (IL-6) and Tumour Necrosis Factor-alpha (TNF-alpha), interferon-gamma (INF-gamma) and serum levels of high sensitive C reactive protein (CRP). In order to test the effects of inflammation on clinical outcome, patients were divided in Non-Responders and Responders according to the Remission criteria of the Schizophrenia Working Group Consensus, measuring a reduction in symptoms severity using the Positive and Negative Syndrome Scale over the first three months of treatment. We also evaluated the association between variation in CRP levels and variation in metabolic variables in a longitudinal study in patients with first episode psychosis.

Results: Patients non-Responders showed significantly higher baseline levels of IL-6 and INF-gamma when compared with Responders. Increases in CRP levels of 3 months follow-up is associated with increase in triglycerides independently by weight gain.

Conclusions: Increased inflammation appears to predict patients with worse clinical and metabolic outcome at the onset of psychosis. Inflammatory markers should be considered for stratification of future therapeutic strategies in first episode psychosis.

Talk 2

Role of Cytokines in Depression and Psychosis and Evidence for Effectiveness of Anti-cytokine Treatment in Depression

Golam Khandaker, Peter B. Jones, Golam Khandaker

Department of Psychiatry, University of Cambridge, Cambridge, UK

Background: I will present evidence from a population-based longitudinal study and a meta-analysis of clinical trials to address whether inflammatory cytokines play a causal role in depression and psychosis, and so could be a therapeutic target.

Methods: The longitudinal relationships between serum IL-6 and CRP levels at age 9 years and subsequent depressive and psychotic symptoms between 10 and 18 years were examined in the Avon Longitudinal Study of Parents and Children (ALSPAC) birth cohort (N = 4415). Secondly, we carried out a systematic review and meta-analysis of antidepressant activity of anti-cytokine treatment (monoclonal antibodies and cytokine inhibitors) using clinical trials of chronic inflammatory conditions where depression was measured as a secondary outcome.

Results: Higher serum IL-6 levels at age 9 years were associated with increased risks of developing depression (OR = 1.55; 95% CI, 1.13-2.14), psychotic experiences (OR = 1.81; 95% CI, 1.01-3.28) and psychotic disorder (OR = 2.40; 95% CI, 0.87-6.62) at age 18 years, and persistent depressive symptoms between 10 and 18 years (OR = 1.19; 95% CI, 1.02-1.39). Random effect meta-analysis of seven RCTs involving 2370 participants showed significant antidepressant effect of anti-cytokine treatment compared with placebo (SMD = 0.39; 95% CI, 0.19-0.60). Meta-regression exploring predictors of response found that the antidepressant effect was associated with baseline depression severity (P = 0.033) but not with improvement in primary physical illness, sex or age.

Conclusions: The findings suggest a potentially causal role for inflammatory cytokines in the pathogenesis of depression and psychosis, and that cytokine modulators may be novel drugs for depression in chronically inflamed subjects.

Talk 3

Evidence for Effectiveness of Immunotherapy in Psychosis

Belinda Lennox

University of Oxford, UK

Advances in pharmacotherapy for psychosis are desperately needed. One potential area for advance is in the repurposing of immune modifying treatments for use in psychosis. For this talk I will review the current evidence base for immunotherapy in treating psychosis. This includes historical studies on the use of steroids to treat schizophrenia, and more recent studies on the use of anti-inflammatory drugs such as Celecoxib (a selective COX-2 inhibitor), which has been reported to improve cognitive function in early stages of schizophrenia, and Minocycline, a centrally acting tetracyclic anti-inflammatory agent which has been reported to improve negative symptoms and cognitive function in schizophrenia. A constant challenge to psychosis research is the heterogeneity of the patient group. Anti-inflammatory drugs will only be effective in those with an inflammatory component to their illness and to date it has been difficult to identify this subgroup of patients. One potential advance has been the description of antineuronal cell surface antibodies in a proportion of people with first episode psychosis. In other presentations with these antibodies, for instance with encephalitis or seizures, patients respond to treatment with immunotherapy, rather than symptomatic treatments. I will report our clinical experience to date of using steroids, intravenous immunoglobulins, plasma exchange and rituximab in the treatment of those with psychosis and antibodies against the NMDA receptor. Of 18 patients treated so far all have improved, and most have achieved remission. However the relevance of antibodies in psychosis,

particularly at low levels, remains controversial, and I will discuss the protocol for a double blind placebo controlled RCT of immunotherapy in patients with psychosis and antibodies that is needed to move the field forwards and confirm whether this should be a new approach for treatment in psychosis.

Talk 4

Immune-related Risk Factors for Schizophrenia and Depression in Danish Epidemiological Studies and Meta-analysis of Anti-inflammatory Treatment for Depression

Michael Benros

Mental Health Centre Copenhagen, University of Copenhagen, Faculty of Health Sciences, Copenhagen, Denmark

Utilizing the extensive Danish Registers we have shown that particularly severe infections requiring hospitalization but also milder infections not requiring hospitalization, and autoimmune diseases were associated with an increased risk of schizophrenia and mood disorders in a dose-response relationship, which seem compatible with an immunological hypothesis for subgroups of the patients. Several studies have indicated antidepressant effects of anti-inflammatory treatment; however, the results have been conflicting and detrimental side effects may contraindicate anti-inflammatory treatment. Hence, we systematically reviewed the antidepressant and possible side effects of anti-inflammatory interventions on individuals with depression. The pooled effect estimate suggested that anti-inflammatory treatment reduced depressive symptoms compared to placebo. This effect was observed both in studies including patients with depression and depressive symptoms. The heterogeneity of the studies was not explained by differences in inclusion of clinical depression versus depressive symptoms or NSAIDs versus cytokine inhibitors. Subanalyses particularly emphasized antidepressant properties for the selective COX-2 inhibitor celecoxib in general, on remission and response. Among the studies reporting on side effects, we found no evidence of an increased number of gastrointestinal or cardiovascular events after 6 weeks or infections after 12 weeks of anti-inflammatory treatment compared to placebo. Hence, our analysis suggests that anti-inflammatory treatment, in particular celecoxib, decreased depressive symptoms without increased risks of side effects. However, a high risk of bias and high heterogeneity made the mean estimate uncertain. Our studies supports a proof-of-concept concerning use of anti-inflammatory treatment in depression and identification of subgroups that could benefit of this intervention is warranted.

Symposium Session 14

Friday, October 21, 1:00–2:30 p.m., Washington B

Early Phases of Bipolar Disorder

Chair: Andreas Bechdolf¹, Co-Chair: Ingrid Melle²

Speakers: Ingrid Melle, Andrea Pfennig, Andreas Bechdolf, Jan Scott
¹Charité Medical University Berlin, Germany, University of Cologne, Köln, Germany, University of Melbourne, Melbourne, Australia, ²University of Oslo, Oslo University Hospital, Norway

The early phases of Bipolar Disorder (BD) demonstrate a range of complex clinical presentations. For example, it is presumed that long duration of untreated BD has a negative impact on illness course and outcome, but evidence is inconsistent and there is limited knowledge about how to define and assess key milestones in untreated BD as compared to psychosis. Likewise, whilst it is possible to differentiate between youth at high risk of developing BD from others with heterogeneous problems, it is unclear if proposed Bipolar-At-Risk (BAR) criteria can differentiate between persons at risk for BD from those at risk for psychosis, or for recurrent unipolar depression. This symposium examines the current state of the art and addresses these issues through presentations of empirical studies of cases of first episode mania and systematic research on different at-risk populations.

Talk 1

Untreated Bipolar Illness and its Association to Outcome in First Episode Mania

Ingrid Melle, Levi Kvitland, Christine Demmo, Sofie Aminoff, Tone Hellvin, Ole Andreassen, Trine Vik Lagerberg, Petter Andreas Ringen

NORMENT, K.G. Jebsen Centre for Psychosis Research, Division of Mental Health and Addiction, Institute of Clinical Medicine, University of Oslo and Oslo University Hospital, Oslo, Norway

Purpose: We have limited knowledge about how aspects of untreated bipolar illness influences clinical outcome in first episode bipolar disorder I (BD I). Half of patients experience one or more depressive episodes before the first defining manic episode. Mood episodes can also be self-limiting with long periods of euthymia in-between. Untreated illness can thus be defined either as the duration of time from the onset of the first mood/manic episode to start of adequate treatment (Duration of Untreated Bipolar Disorder, DUB) or as the number of untreated mood/manic episodes. The present study examines the associations between aspects of untreated illness in BD-I and key clinical outcomes.

Method: Patients (N = 62) were recruited at first adequate treatment for mania, and followed-up after one year with comprehensive assessments at both time-points.

Results: There were no significant associations between DUB and key clinical outcomes neither at baseline nor at one-year follow-up. The same was the case for associations to the number of untreated mood/manic episodes. Longer time from first mania to adequate treatment was associated with higher risk of post-onset excessive cannabis use.

Conclusion: The initial phases of early bipolar disorder have a complex clinical presentation with uncertain links to clinical outcome. We need better assessments to capture important aspects of this period

Talk 2

Symptom Constellations and Health Care Experiences in Bipolar-At-Risk

Andrea Pfennig¹, Steffi Pfeifer¹, Michael Bauer¹, Karolina Leopold^{1,2}

¹Department of Psychiatry and Psychotherapy, Carl Gustav Carus University Hospital, Technische Universität Dresden, Germany,

²Department of Psychiatry, Psychotherapy and Psychosomatics, Vivantes Klinikum am Urban, Academic Hospital of Charité Medicine Berlin, Berlin, Germany

Purpose: Most young subjects considered at heightened risk to develop bipolar disorder already suffer from severe symptomatology and functional impairment even without the manifestation of full-blown bipolar disorder. For a number of reasons, the identification of high-risk subjects is difficult but it is crucial to provide them with the appropriate counselling and, if needed, treatment. We here aim at describing the symptom constellations of patients and their health care experiences prior and after visiting the Early Recognition Centre of our Mental Health Centre.

Method: A structured diagnostic process was applied to clients visiting the Early Recognition Centre including two instruments developed to detect a heightened risk for bipolar disorder (BPSS and EPIbipolar). Retrospective and prospective data on diagnoses, contacts to the health care system and treatment approaches were collected prospectively for six years. Conversion to manifest disorders was assessed using standardized diagnostic instruments.

Results: Data from 660 clients (12 to 40 years old) visiting the Early Recognition Centre were analysed. About 15% of those seen in comprehensive diagnosis visits (about 400) were meeting the research criteria for heightened bipolar risk. Symptom constellations including disturbances in sleep and circadian rhythm and mood swings including euphoric states leading up to mania prodrome will be described. Most patients had prior contacts with the health care system that were frustrate. Follow-up including conversion data will be presented.

Conclusions: In light of the results, the importance of specialized early recognition and intervention centres will be discussed.

Talk 3

Predictive Validity of Bipolar At Risk (BAR) Criteria

Andreas Bechdolf^{1,2,3}, Aswin Rateesh^{2,4}, Sue M Cotton^{2,4}, Jennifer Betts^{2,4}, Andrew Chanen^{2,4}, Barnaby Nelson^{2,4}, Michael Berk^{4,5,6}, Patrick D McGorry^{2,4}

¹Department of Psychiatry, Psychotherapy and Psychosomatics, Vivantes Klinikum am Urban, Early Intervention and Treatment Center – FRITZ am Urban, Charité Medical University, Berlin, Germany, ²Centre for Youth Mental Health, University of Melbourne, Parkville, Australia, ³Department of Psychiatry and Psychotherapy, University of Cologne, Cologne, Germany, ⁴Orygen, The National Centre of Excellence in Youth Mental Health, Parkville, Australia, ⁵Deakin University, Geelong, Australia, ⁶Florey Institute of Neurosciences and Mental Health, Parkville, Australia

Purpose: We developed the Bipolar-At Risk criteria (BAR) which include being at peak age range of the onset of the disorder, as well as a) sub-threshold manic features, b) presence of subthreshold depression with cyclothymic features and c) presence of subthreshold depression in combination with genetic risk. The primary aim of the present study was to determine the predictive validity of the BAR criteria. Moreover, we aimed to examine the relationship between BAR criteria and other clinical syndromes associated with bipolar risk.

Method: Twelve-month prospective trial. Baseline measures included substance- and antidepressant use, Attention Deficit Hyperkinetic Disorder (ADHD), Borderline personality disorder (BPD) and temperamental traits, criteria for Ultra-High Risk for psychosis (UHR) and the Bipolarity Index to determine relationships between concepts.

Results: Thirty-five participants were included in the BAR group and 35 matched participants in the control group. Five BAR patients (14.3%) converted to first-episode hypomania/mania and none in the non-BAR group [$\chi^2(1) = 5.38, p = 0.020$]. Baseline BAR criteria were associated with higher scores on Bipolarity Index, Young Mania Rating Scale, Brief Psychiatric Rating Scale, TEMPS-A and its cyclothymic subscale. It was also associated with more baseline cannabis use disorder diagnoses. BAR criteria were not associated with UHR criteria, Brown ADD scores and BPQ scores.

Conclusions: BAR criteria present with clinical relevant conversion rates into bipolar disorder and with expected overlap with mania symptoms and cyclothymic traits, without overlap with risk for psychosis, ADHD and BPD. Cannabis use may represent a distal additional risk factor.

Talk 4

Strategies to Identify Individuals at High Risk of Developing First Episode Mania

Jan Scott

Institute of Neuroscience, Newcastle University, Newcastle upon Tyne, UK

Purpose: Bechdolf and colleagues developed a bipolar disorder (BD) 'at-risk' assessment tool for use with help-seeking individuals. The BAR assessment incorporates general and specific criteria that can be used to identify those at high risk of developing BD: cyclothymia, sub-threshold mania, depression and genetic risk. Utilisation of these criteria in early intervention services have been promising. A specific challenge is not just their ability to identify BD at risk cases from young people with heterogeneous problems, but also to determine which individuals are at risk of imminent 'transition' to BD from populations comprised of early onset depression cases. This is of great importance clinically and a significant challenge to the utility of the BAR criteria. The present study addresses this issue and reports on the validity of the BAR criteria in differentiating early onset BD from UP.

Method: A sample of 100 cases matched for gender and year of birth were followed prospectively after participating in systematic screening assessments for a different research studies in the UK.

Results: We examine additional criteria that may be particularly important in identifying those at risk of mania from large populations of young adults with recurrent depression (e.g. symptoms of activation or fatigue). Finally, taking all this information together, the presentation provides an estimate of the 'Number needed to screen' (NNS), a parameter for case finding that can be used by clinicians to determine how likely they are to identify cases of first episode mania in a given clinical population.

Symposium Session 15

Friday, October 21, 1:00–2:30 p.m., Manzoni

Vulnerability to the Effects of Cannabis on Transition to Psychosis

Chair: Katherine Aitchison¹, Co-Chair: Robin Murray²

Speakers: Robin M Murray, Philip Tibbo, Jean Addington, Tamar Kraan

¹Departments of Psychiatry and Medical Genetics, University of Alberta, Alberta, Canada; King's College London, Institute of Psychiatry, Psychology & Neuroscience, London, UK, ²Institute of Psychiatry, Psychology & Neuroscience, Department of Psychosis Studies, King's College London, London, UK

While several vulnerability factors for transitioning to a psychotic illness after consumption of cannabis have been described, there are inconsistencies in the data. For example, there has been some difficulty in replicating the findings of Caspi et al (2005). This symposium focuses on delineating genetic, environmental, and demographic factors that contribute to the transition to a psychotic illness. The first speaker, Robin Murray (Institute of Psychiatry, London), will discuss cannabis, and its ingredient THC, as a risk factor for psychosis and cognitive dysfunction, and compare and contrast patients with an "At Risk Mental State" to first episode psychosis patients. The second speaker, Phil Tibbo (Dalhousie University, Halifax, Canada), will report on a Canadian sample in which, consistent with Caspi et al (2005), COMT genotype was seen to have a significant effect on age of onset of psychosis, in those who had first used cannabis at less than or equal to 19 years of age. The third speaker, Jean Addington (University of Calgary, Canada), will present data on cannabis use in those in a clinical high risk state and association with symptoms and subsequent conversion to psychotic illness. The fourth speaker, Tamar Kraan (Amsterdam, NL) will review the data on cannabis use and transition to psychosis in individuals at ultra-high risk for psychosis. Unpublished data will be included. In summary, this symposium will shed light on the complexity regarding the association between cannabis and subsequent development of a treatable psychotic illness, with clear implications for public health education and prevention.

Talk 1

The Role of Cannabis Use and Individual Susceptibility in Influencing Outcome Among Patients with A) The ARMS and B) Frank Psychosis

Robin M Murray¹, Tabea Schoeler¹, Daniel Friedman², Elizabeth Tunbridge², Olesya Ajnakina¹, Marta Di Forti²

¹King's College London, London, UK, ²University of Oxford, Oxford, UK

Strikingly, all nine longitudinal prospective studies of young people in the general population have shown that those who use cannabis have a greater risk of developing psychosis than non-users. Of course, only a minority of cannabis users will develop psychosis. Some people appear genetically susceptible; at least three genes are implicated: DRD2, AKT1, and COMT. Our experimental studies have demonstrated that IV administration of tetrahydrocannabinol (THC) can readily induce a transient psychosis in normal volunteers. In a recent study of 78 schizotypal individuals, we examined whether the COMT Val/Met genotype moderated THC-induced paranoia. This did not occur, rather, a greater impairment of working memory resulted in those of COMT Val/Val genotype. In a meta-analysis, we found that those psychotic individuals who continue to use cannabis have a worse outcome with higher relapse rates, more hospitalisations, and more continued positive symptoms than both those former users who stop their use and also psychotic patients who never used cannabis. In considering whether cannabis use influences risk of transition in individuals with an ARMS, it is important to address the question of how representative such individuals are of FEPs. Our evidence is that only about 5% of FEP in South London have attended prodromal services with an ARMS and that those who have differ in that they were more likely to have been referred by general practitioners, live with their family and be born in the UK than the majority of FEP; they did not, however, differ significantly in their use of cannabis.

Talk 2

COMT Genotype is Associated with Age of Onset of Psychosis After Adolescent Cannabis Use: A Replication in Canadian Caucasians

Philip Tibbo^{1,2}, Katherine J Aitchison^{3,4,5}, Rohit J. Lodhi³, Yabing Wang³, Alexandra Loverock⁵, Aleksandra Dimitrijevic³, Candice Crocker¹, Hongyan Ren³, Darren Bugbee³, Georgina Macintyre³, Scot E Purdon^{3,4,6}

¹Dalhousie University, Halifax, Nova Scotia, Canada, ²Nova Scotia Early Psychosis Program, Canada, ³University of Alberta, Edmonton, Alberta, Canada, ⁴Edmonton Early Psychosis Intervention Clinic, Alverta, Canada, ⁵Northern Ontario School of Medicine, Sudbury, Ontario, Canada, ⁶Alberta Hospital Edmonton, Canada

Background: While several vulnerability factors for transitioning to a psychotic illness after consumption of cannabis have been described, there are inconsistencies in the data. For example, there has been some difficulty in replicating the findings of Caspi et al (2005).

Methods: Patients of self-reported Caucasian ethnicity with psychosis were recruited from two first episode psychosis teams, in Edmonton, and Halifax (Canada), and a collaborating hospital. Age of onset of psychosis (AoP), defined as age of DSM-IV diagnosis (schizophrenia, schizoaffective disorder, schizophreniform disorder, delusional disorder, brief psychotic episode, psychosis not otherwise specified, and substance-induced psychosis) was established using the Structured Clinical Interview for DSM-IV. Data on cannabis use were collected using a self-report computerized questionnaire. DNA was extracted from saliva collected using Oragene kits. The COMT Val158Met variant (rs4680) was genotyped by SNaPshot and Taq-Man assays.

Results: COMT genotype was associated with lifetime cannabis use and with age of first cannabis use. In those who had used cannabis ≤ 19 years of age, COMT genotype had a significant effect on AoP.

Conclusion: Our data are consistent with those of Caspi et al (2005), which may reflect factors such as Caucasian ethnicity (confirmed using ancestry informative markers), and other sociodemographic factors. Funding: Bebensee Schizophrenia Research Unit, Canadian Institutes of Health Research (grant 200810), Nova Scotia Health Research Foundation, Canadian Foundation for Innovation, Alberta Innovation and Advanced Education, Government of Alberta (Alberta Centennial Addiction and Mental Health Research Chair to KJA).

Talk 3

Cannabis Use in Individuals at Clinical High Risk of Psychosis

Jean Addington¹, Kristin S Cadenhead², Tyrone D Cannon³, Barbara A Cornblatt⁴, Thomas H McGlashan³, Diana O Perkins⁵, Larry J Seidman^{6,7}, Elaine F Walker⁸, Scott Woods³, Carrie E Bearden¹⁰, Daniel Mathalon¹¹, Lisa Buchy¹

¹University of Calgary, Alberta, Canada, ²University of California, San Diego, CA, USA, ³Yale University, New Haven, CT, USA, ⁴Zucker Hillside Hospital, New York, USA, ⁵University of North Carolina, USA, ⁶Harvard Medical School at Beth Israel Deaconess Medical Center, Boston, MA, USA, ⁷Massachusetts General Hospital, USA, ⁸Emory University, Atlanta, GA, USA, ⁹National Institutes of Mental Health, Bethesda, MD, ¹⁰University of California, Los Angeles, CA, USA, ¹¹University of California, San Francisco, CA, USA

It has been suggested in the literature that cannabis use may have an impact on the later development of psychotic symptoms. This presentation will focus on cannabis use in youth at clinical high risk (CHR) of developing psychosis.

Method: The sample consisted of 735 CHR youth and 278 healthy controls. All participants were recruited as part of the 8-site North American Prodrome Longitudinal Study (NAPLS-2) and met criteria for a clinical high risk syndrome based on the Structured Interview for Prodromal Syndromes. Sample were assessed at baseline, 6, 12, 18 and 24 months. Measures included the SCID, the Scale of Prodromal Symptoms, the Alcohol and Drug Use Scale plus some additional questions about cannabis use.

Results: Cannabis was the most widely used drug in both CHR and control groups. Cannabis use was significantly higher in the CHR group than in the controls and use did not change over time. Increased use was significantly associated with higher ratings on attenuated psychotic symptoms. The CHR group was significantly younger than controls when they first used and had used more often across their lifetime. CHR youth were more likely to currently use alone and during the day compared to controls. Those who later converted to psychosis demonstrated using slightly more cannabis than those who did not.

Conclusion: Although there are limitations to the data those at CHR had increased use of cannabis compared to controls and for those at CHR there was an impact of cannabis on their symptoms.

Talk 4

Current Cannabis Abuse is Associated with Transition to Psychosis in Individuals at Ultra-high Risk for Psychosis

Tamar Kraan¹, Eva Velthorst^{1,2}, Laura Koenders¹, Kimberley Zwaart^{3,4}, Helga K Ising⁴, David van den Berg⁴, Lieuwe de Haan¹, Mark van der Gaag^{3,4}

¹University of Amsterdam, The Netherlands, ²Mount Sinai, New York, USA, ³VU University, Amsterdam, The Netherlands, ⁴Parnassia Psychiatric Institute, The Hague, Netherlands

Background. Cannabis is the most used drug worldwide. The use of this drug has been widely associated with psychotic disorders. The present study aimed to review the existing literature on the association between cannabis use and transition to psychosis in UHR samples.

Method: We reviewed the literature on all available prospective studies on cannabis use in UHR cohorts. Out of 5559 potentially relevant articles, 36 articles were screened on full text for eligibility. Two random-effects meta-analyses were performed. First, we compared transition rates to psychosis of UHR individuals with lifetime cannabis use with non-cannabis-using UHR individuals. Second, we compared transition rates of UHR individuals with a current DSM-IV cannabis abuse or dependence diagnosis with lifetime users and non-using UHR individuals.

Results: We selected seven studies that reported on lifetime cannabis use in prospective UHR cohorts ($n = 1171$). Of these seven studies, five studies looked into cannabis abuse or dependence. Using meta-analytical techniques, we found that lifetime cannabis use was not significantly associated with transition to psychosis [odds ratio (OR) 1.14, 95% confidence interval (CI) 0.856–1.524, $p = 0.37$]. Examining cannabis abuse or dependence, an OR of 1.75 (95% CI 1.135–2.710, $p = 0.01$) was found, indicating a significant association between current cannabis abuse or dependence and transition to psychosis.

Conclusions: Our results show that cannabis use was only predictive of transition to psychosis in those who met criteria for cannabis abuse or dependence, tentatively suggesting a dose-response relationship between current cannabis use and transition to psychosis.

Symposium Session 16

Friday, October 21, 1:00–2:30 p.m., Foscolo

Similarities and Differences of Early Intervention Programs in Italian Regions

Chair: Walter Di Munzio¹, Co-Chair: Andrea Alpi²

Speakers: Anna Meneghelli, Angela Carofiglio, Marco Vaggi, Giuliano Limonta

¹Dipartimento di Salute Mentale, Salerno 1, ASL Salerno, Salerno, Italy,

²Programma 2000, Milan, Italy

The symposium, organized by the AIPP (Italian Association for Prevention and Early Intervention in Mental Health) and dedicated to the memory of Angelo Cocchi, is aimed at describing some relevant and paradigmatic EI experiences within the Italian context. Four services, implemented at different moments and within different geographic and organizational contexts, that share however orientation and objectives, are described. "Programma 2000", a specific service in MHD of Niguarda, Milan, has been since late 90s' the first national leading service for the development of this area, regarding treatment as well as research. The GIPPSI Project in Bari, a city located in

Southern Italy, with more than 300,000 inhabitants, has followed the same model, using an original collaboration among MHD and private-social subjects. CSM in Genova Voltri, is a generalist service addressed to an area with 100,000 inhabitants (in a city with 600,000 inhabitants) located in Northern Italy, where a dedicated group, with specialized workers, has been operating since 2003. DSM in Piacenza, a city in Northern Italy with 100,000 inhabitants, has adopted the model of a dedicated service in a generalist context. However, it operates within the whole Mental Health Department territory, contrarily to the one in Genova. Contributions show that sharing references and the strong motivation, in a country like Italy, where the National Health Care Service (SSN) is run by Regions through local models, are trying to allow the activation of focused interventions of prevention and treatment of young individuals adapting the organization to specific situations.

Talk 1

Programma 2000: A Leading Model for the Early Intervention Paradigm in Italy

Anna Meneghelli¹, Emiliano Monzani¹, Antonio Preti^{1,2}, Mariano Bassi¹

¹Programma 2000 Milan, Italy, ²University of Cagliari, Cagliari, Italy

Purpose: To illustrate the organization, functioning and main outcomes of the Programma2000, the first multi-modal, comprehensive program targeted at the early detection and intervention for persons at the onset and for those with a high risk of psychosis established in Italy in 1999.

Materials and Methods: All patients who are referred to Programma2000 receive a prompt admission in treatment (within 24 h), and undergo a comprehensive, multidimensional evaluation with a package of standardized assessments. Those who comply with the criteria for diagnosis are proposed an individualized, multicomponent protocol of treatment including evidence-based drug and psychosocial treatments and a wide range of therapeutic support group activities.

Results: Over 16 years of activity, the Programma2000 assessed over 500 subjects, 302 of whom were entered in treatment. Treatment appears effective in reducing morbidity and improving social functioning. About 2/3 patients with first episode of psychosis achieved remission after 1 year, with 67% being in remission at 3 years. Transition to psychosis was limited to 5% of patients at ultra high risk of psychosis. The Programma2000 actively promoted the knowledge of the early intervention paradigm, with conferences, congresses, scientific publications and national surveys.

Conclusion: Programma2000 gained a respected leadership role as a referent model for the creation of early intervention services. The effort of establishing a fidelity model for the early intervention protocol of care resulted in 2014 in a proposal of a general reform of the Italian Department of Mental Health, aimed at spreading a preventative approach to mental distress.

Talk 2

Model-conformity and Field Testing: GIPPSi, an Original Experience of "Center Specifically Dedicated to FEP and HR"

Angela Carofiglio¹, Cristina Filograno², Elvira Damato², Francesca Gatti², Rosa Marinelli², Annamaria Piperis², Gerolamo Stea², Daria Portnova², Giuseppe Verrastro¹, Domenico Semisa¹

¹Mental Health Department - ASL Bari, Italy, ²Foundation EPASSS (ACLI Institution Provincial Social Services-Health), Italy

In 2010 a small group of professionals, basing on the model of Programma 2000, decided to launch a centre dedicated to onset of psychosis, first centre of this kind in Apulia and Southern Italy. The centre immediately adopted problem solving as procedure to face obstacles, which allowed to use the resources of the context as effectively as possible. Starting with an uncommon close cooperation between "public" and "private", the centre chose to benefit from the resource of a pre-existing daily-care centre, employing its physical spaces and specialized experts in psychiatric rehabilitation, in order to launch a care-service focused on the process of individuation and promotion of autonomy in young individuals. Components recommended by guidelines (Nice-ISS 2007), in particular individual CBT, intervention on families and recovery of social functioning, have been preserved, within a work based on extreme flexibility and inclusiveness. The transition to taking care of HR was natural and prompted us to set up an intervention protocol specifically addressed to young subjects facing this condition. At the end of 2015, GIPPSi has scored 180 diagnostic assessments, taken on responsibility of 37 FEP and 33 HR, discharged 13 young subjects who had successfully completed their individual therapeutic project.

Talk 3

Implementation of a Prevention and Early Intervention Clinical Service in a Mental Health Community Center of Genoa, Italy

Marco Vaggi¹, Eugenia Perelli¹, Valeria Puppo¹, Monica Zambonini¹, Panfilo Ciancaglini²

¹Department of Mental Health and Substance Abuse, ASL3 Genoa, Italy,

²Italian Association for Prevention and Early Intervention in Mental Health (AIPP)

Aim: The work describes the organizational changes of a not specialized Mental Health Centre (CSM) in Genoa (Italy), inspired by the principles of Early Psychosis and by the "Memo for the Mental Health Services development oriented to prevention and focused on young people" by AIPP.

Method: The fundamental principles of the change have been: 1. the cooperation with the general practitioners (MMG) and the services for teenagers 2. evaluation visits differentiated by age groups (<25, 25-65, >65) 3. the identification of specific treatments for different pathologies and the related "specialization" of health workers 4. the creation of a group dedicated to early intervention 5. the gradual shift of resources to young patients. The reallocation of resources has been made possible thanks to the creation of a psychogeriatric service, to the rationalization of the assistance to patients suffering from persistent pathologies and to the limitation of in-house treatments. The second section shows the treatment plans and the monitoring of under 25 aged patients, who started using the services for the first time between Jan. 1st, 2012 and Dec. 31st, 2015.

Results: The course of treatment following the first visit of two hundred and fifty patients (126 males and 124 females) was analysed and five groups were identified: 53 cases (21%) followed by multi-professional teams, 43 cases (17%) treated by one unit (or centre), 37 cases (15%) watched with an active clinical follow up, 85 cases (34%) monitored, 32 cases (13%) sent to different public health care agencies.

Talk 4

Stand UP Project Addressed to Onset of Psychosis in the Network of the Standardized Instrument PTDA (Diagnostic Therapeutic And Assistance Pathway) of Piacenza Mental Health Department

Giuliano Limonta

Mental Health and Pathological Addictions Department - AUSL Piacenza, Italy

Premise: An organizational model focused on institutional setting and treatment centres rather than on the patient, exposes to the risk of fragmented interventions, poor adherence to treatment and difficult outcome evaluation.

Method: The model of combined therapeutic functions, structured within a path, promotes interventions enhancing and reinforcing good practice, sharing specific and global treatment objectives within the team. The Mental Health and Pathological Addictions Department of AUSL Piacenza has undertaken a gradual and radical transformation of traditional organizational models (Simple or Complex Operating Unit), using the PTDA model on different specific pathologies, including onset of psychosis. According to this model, PTDA become a sort of "underground network" that enhances, replaces and inspects traditional institutions in the territory (Services and Operating Units of DSMDP), facilitating a radical reorganization of Health Care Services. More specifically on 288.980 inhabitants, among them about 5.775 (3,2% of target aged 18-65 referring to MHC, whereas 2.818 (7,1% of target aged 0-17 referring to CAMHS).

Results: In each MHC teams dedicated to treatment of onset of psychosis have been planned; they are made of professionals trained in CBT and family psychoeducation, including: psychiatrists, child psychiatrists, psychologists, social workers, educators, nurses. PTDA were realized after the implementation of an educational path started in 2011, still in progress: a high - quality, effective path, efficient in increasing knowledge, operational skills and self-efficacy as essential requisites in order to get to "know-how" and to an appropriate empirical consequence of the learnt contents.

Question and Answer Period

Discussant: Maximilian Birchwood, University of Warwick, Coventry, UK

Symposium Session 17

Friday, October 21, 1:00–2:30 p.m., Parini

Research and Management Approaches to Psychosis Onset and Substance Abuse: From Behavioural Neurosciences to Real Clinical Life

Chair: Carlo Altamura¹, Co-Chair: Anita Riecher-Rössler²

Speakers: Stefan Borgwardt, Fabrizio Schifano, Paolo Brambilla, Marta Di Forti

¹University of Milan, Italy, ²Universitäre Psychiatrische Kliniken (UPK), Basel, Switzerland

It is important to evaluate the impact of substance abuse on onset and course of psychosis, as regular use of drugs can move up the age of onset of prodromal symptoms, or first episode psychosis, and worsen the manifestation of psychotic symptoms in those adolescents who use them regularly, with particular regards to cannabis. In this symposium we will illustrate the major research and management approaches to psychosis and substance abuse, including both the fields of behavioural neurosciences and real clinical life. First, major UK and European studies will be presented to discover if and how variations in cannabis use, in different countries, can explain their variations in the Incidence of Schizophrenia and other Psychosis. Then, imaging studies on affective and schizophrenia psychosis and comorbid substance abuse will be presented; in fact, structural and functional magnetic resonance imaging (MRI) studies have identified robust changes in brain structure and activity during the early development of psychosis, but the contribution of substance use around the onset of schizophrenic psychosis is unclear. Finally, convenors will be provided with a range of information relating to most recent prevention and treatment approaches in terms of both 'classical' and more recent drugs of misuse. In conclusion in this symposium we will try to enlighten whether adolescent initiation of substance abuse use is associated with emergence and severity of psychotic symptoms, functional impairment and brain alterations, particularly for adolescents at high risk for developing a psychotic disorder. Also, we will deepen actual treatment and prevention approaches.

Talk 1

Imaging of Early Schizophrenic Psychosis and Substance Abuse

Stefan Borgwardt

University of Basel, Basel, Switzerland

Structural and functional magnetic resonance imaging (MRI) studies have identified robust changes in brain structure and activity during the early development of psychosis, but the contribution of substance use around the onset of schizophrenic psychosis is unclear. We report single study and meta-analytical results of studies comprising healthy users and non-users with respect to drug related alterations on the white and grey matter structures as well as brain activity changes. We then systematically reviewed structural and functional brain imaging and post mortem studies addressing the effects of drugs use on brain structure and function in schizophrenic psychoses. The aim of this presentation is to discuss whether the healthy brain, chronic and long-term drug exposure may exert significant effects in specific brain areas and whether while early psychosis patients might be particularly vulnerable to brain volume and function alterations due to drug use exposure.

Talk 2

Prevention and Treatment of Substance Abuse

Fabrizio Schifano

University of Hertfordshire, Hatfield, UK

During the presentation, convenors will be provided with a range of information relating to most recent prevention and treatment approaches in terms of both 'classical' and more recent drugs of misuse. Over the last 10 years or so, many NPS have become available. These are advertised via the Internet as being safer and legal alternatives to illicit drugs. However, information on their effects is minimal or inaccurate. They can be just as harmful and addictive as illegal drugs such as cocaine, ecstasy or ketamine. The regular development of further NPS, combined with the web ability to spread information quickly, presents with a number of challenges for public health across the globe. The products are just a 'click away' from our homes and thus potentially available to everyone, especially young people who are amongst the most at risk. Convenient labelling of NPS maintains that they are "not for human consumption", this loophole sometimes allowing them to be distributed cheaply, remain legal and easy to obtain. Popularity of the NPS is on the increase because of the advantage to users of the incapacity of the standard drug tests to identify them. Without the knowledge of the NPS pharmacological/toxicological profile, however, their use is to be considered dangerously experimental, good effects serendipitous. Many of the NPS are research chemicals, sometimes even discarded products from drug research. They are produced mainly in Asian countries and usually on a large scale.

Talk 3

Imaging of Bipolar Disorder and Substance Abuse

Paolo Brambilla

University of Milan, Milan, Italy

Bipolar Disorder (BD) is commonly characterized by the presence of psychotic symptoms and by the co-occurrence of substance use, features which may act to exacerbate its clinical manifestation. However, the specific role and the neurophysiological correlates of co-morbid substance abuse remain unclear. Therefore, this study aims at identifying diagnosis-specific structural and metabolic alterations within fronto-temporal and striatal regions differentiating psychotic BD patients with or without substance abuse and substance-induced psychotic patients, coupling MRI and Positron Emission Tomography (PET) approaches. BD type I psychotic patients with and without substance abuse, and healthy controls were enrolled in this study. MR images were acquired using a 3-Tesla MRI scanner and patients further underwent 18-FDG-PET scanning. The group analyses reported a common pattern of GM volumes and metabolic abnormalities in several fronto-temporal and striatal regions in affected patients compared to healthy controls. Also, diagnosis-specific abnormalities emerged from our results. Our findings suggest that the exposure to substance of abuse may alter, both structurally and metabolically, selective brain structures which, in turn, may lead to the identification of specific biomarkers associated with the neurotoxic effects of substance of abuse.

Talk 4

Cannabis Use Across the EU: A Ticket to Psychosis?

Marta Di Forti

IOPPN, King's College, London, UK

Between May 1, 2005, and May 31, 2011, we obtained data from 410 patients with first-episode psychosis and 370 population controls. The risk of individuals having a psychotic disorder showed a roughly three-times increase in users of skunk-like/high potency cannabis and over 5 times in daily users of high potency cannabis compared with those who never used cannabis. The population attributable fraction of first-episode psychosis for skunk-like/high potency cannabis use for our geographical area was 24% (95% CI 17–31), possibly because of the high prevalence of use of high-potency cannabis (218 [53%] of 410 patients) in our study (Lancet Psychiatry, 2015). We concluded that the ready availability of high potency cannabis in south London might have resulted in a greater proportion of first onset psychosis cases being attributed to cannabis use than in previous studies. Moreover, we know that the distribution of environmental risk factors can significantly vary across different countries resulting in geographical differences in the incidence of complex diseases. Therefore, we measured differences in prevalence and pattern of cannabis use across 5 European countries and to investigate whether this resulted in differences in the proportion of new cases of psychosis attributable to cannabis use across Europe. I shall start presenting our South London GAP study findings. Then I shall take you on the EU GEI-study train for a “preview” trip across the EU to discover if and how variations in cannabis use, in different countries, can explain their variations in the Incidence of Schizophrenia and other Psychosis.

Symposium Session 18

Friday, October 21, 2:45–4:15 p.m., Washington A

New Targets for Prevention of Schizophrenia: Is it Time for Interventions in the Premorbid Phase?

Chair: Larry J. Seidman¹, Co-Chair: Merete Nordentoft²

Speakers: Larry Seidman, Rudolf Uher, Nicoline Hemager, Matcheri Keshavan

¹Harvard Medical School, Massachusetts General Hospital, Boston, MA, USA, ²Institute for Clinical Medicine, University of Copenhagen, Copenhagen, Denmark

A number of influences have converged suggesting that the time is right for primary prevention strategies with interventions in the premorbid phase of schizophrenia. These factors include: 1. There is substantial knowledge about premorbid developmental vulnerabilities to psychosis, especially regarding schizophrenia. Data from family high-risk (FHR) studies indicate that in addition to a 10% risk for psychotic disorders, these children run a 50%–60% risk for significant difficulties including nonpsychotic psychopathology, socio-emotional, cognitive, neuromotor, and speech-language problems. Thus, while these children are preprodromal, they are not unaffected. 2. The promising results emerging from interventions during the clinical high-risk (CHR) phase of psychosis give hope that earlier interventions are possible. 3. There is recognition that the CHR period is a relatively late phase of developmental derailment. These factors have together led to a perspective that even earlier intervention is warranted. While the FHR approach was originated in the 1950's, it was not until recently, that interventions have begun to be initiated. A new round of FHR studies has focused on preteen

offspring or siblings of people with schizophrenia or bipolar disorder, starting as early as ages 7–9 years. We bring together 4 active studies that address these issues in Pittsburgh (Keshavan) and Boston (Seidman) in the United States, Halifax, Canada (Uher) and Copenhagen, Denmark (Hemager). These authors will document the clinically meaningful dimensions that will be targeted in interventions, and the nature of planned interventions. We will discuss ethics, safety, potential stigma, feasibility, tolerability, and the meaning to the people involved.

Talk 1

Family Structure, Behavior and Symptoms in Young Children at Familial Risk for Schizophrenia

Larry Seidman¹, Elena Molokotos¹, Benjamin Brent¹, Ashley Ronzio¹, Eugene D'Angelo¹, Joanne Wojcik¹, Raquelle Mesholam-Gately¹, Cindy Liu¹, Matcheri Keshavan¹, John Gabrieli¹

¹Harvard Medical School, Boston, MA, USA, ²Massachusetts Institute of Technology, Boston, MA, USA

Objective: To evaluate function in parents with schizophrenia, and behaviour in their offspring.

Methods: Using a family high-risk (FHR) design, we evaluated 20 non-psychotic, offspring of parents with psychotic disorders (HRP), contrasting them with 30 non-psychotic controls (CON) without any first-degree relatives with psychosis. The mean age of the child sample was 9 years (range 7–12).

Results: Preliminary analyses on the first half of the sample were revealing. Of the first 10 families, 70% of the ill parents were mothers, 20% were fathers, and 10% were siblings. In virtually all of these families, the mother was the primary caretaker, and in only two families was there a partner. Mothers were primarily from lower socio-economic status and often conveyed a sense of being overwhelmed economically and emotionally. More than half of the children met criteria for ADHD and/or oppositional defiant disorder. The children were significantly impaired on all dimensions of the BRIEF including the Executive Composite ($P = .003$). They were also significantly impaired on many dimensions of the CBCL including both Internalizing and Externalizing Problems. The HRP children did not show significant differences on scales of Magical Thinking or Psychotic-Like Experiences.

Conclusion: These results demonstrate that significant behavioural difficulties are present in pre-teen HRP children, especially in aspects of executive control of behaviour, and not in pre-psychotic experiences. Also striking was the sense of being overwhelmed in the parents. These preliminary results suggest interventions building social support for the parents to reduce stress and help build structure for their children.

Talk 2

Skills for Wellness: An Early Intervention to Pre-empt Mood and Psychotic Disorders in Non-treatment Seeking High-risk Youth

Rudolf Uher, Barbara Pavlova, Alim Awadia, Alexa Bagnell, Sabina Abidi, Alisa Pencer, Jason Morrison

Dalhousie University, Halifax, Canada

Family history and psychopathological antecedents may help target early interventions to those at risk for severe mental illness, but most youth with early psychopathology do not seek treatment. We have developed Skills for Wellness (SWELL) as a cognitive-behavioural pre-emptive intervention for non-treatment seeking youth. We are testing the acceptability and effectiveness of SWELL in a randomized controlled trial embedded within a high-risk cohort of youth aged 9 to 21 years. The Families Overcoming Risks and Building Opportunities for Well-being (FORBOW) cohort including 234 sons and daughters of parents with major depressive disorder, bipolar disorder or schizophrenia (family high risk, FHR) and 66 offspring of parents with no major mood or psychotic disorders (comparison offspring, CO). We annually assess four putative antecedents that may precede and predict severe major illness: affective lability (present in 34% FHR and 17% CO), anxiety (32% FHR, 15% CO), psychotic symptoms (20% FHR and 9% CO) and basic symptoms (20% FHR and 9% CO). Youth presenting with one or more of the antecedents are eligible for SWELL. SWELL is delivered by a psychologist in 8-16 individual sessions. In addition to core elements including emotion knowledge, realistic thinking, problem solving and present moment focus, modules addressing affective lability, anxiety and psychotic/basic symptoms are selected to fit each participant's risk profile. At the time of writing, 34 youth have been randomized. Of the 17 youth allocated to SWELL, 14 (82%) completed the intervention, suggesting high acceptability. Testing of effectiveness is in progress

Talk 3

Cognitive Profiles in 7-Year-Old Offspring of Parents with Schizophrenia or Bipolar Disorder

Nicoline Hemager¹, Jens Jespen¹, Camilla Christiani¹, Anne Thorup¹, Ditte Ellersgaard¹, Katrine Spang¹, Birgitte Burton¹, Maja Gregersen¹, Anne Ranning¹, Aja Greve¹, Ditte Gantriis¹, Kate Kold¹

¹University of Aarhus, Denmark, ²University of Copenhagen, Denmark

Schizophrenia (SZ) and bipolar disorder (BD) are severe, complex neurodevelopmental disorders with multifactorial etiology of interacting genetic and environmental factors. One of the aims of the Danish High Risk and Resilience Study – VIA 7 is to characterize neurocognition, social cognition and social functioning of 7-year-old offspring with familial high risk for SZ (FHR-SZ) or BD (FHR-BD) and compare them with control offspring without FHR for these disorders (FHR-C). We hypothesize that the FHR-SZ and FHR-BD groups will show impairments in neurocognition and social cognition and display lower social functioning compared to the FHR-C group. The FHR-SZ group is expected to show more pronounced impairments than the FHR-BD group. The aim is to describe profiles of impairments across the following domains: general intelligence, processing speed, language, memory, attention, executive function, Theory of Mind and emotion recognition. We established a stratified cohort of 522 7-year-old offspring recruited on the basis of parental diagnosis in the register: Subgroup 1: 202 children with 1 or 2 parents with SZ. Subgroup 2: 120 children with 1 or 2 parents with BD. Subgroup 3: 200 children of parents with no history of SZ or BD matched with subgroups 1 and 2 on age, gender, and municipality. The domains are measured with a comprehensive test battery of standardized individual assessment methods and questionnaires. Analyses are ongoing and will be presented. Identifying cognitive profiles enables an integrative perspective on impaired and intact cognitive abilities and has potential implications for early intervention and prevention strategies in the FHR groups.

Talk 4

Poly-enviromic Scores Predict Psychosis in Adolescents at Familial High Risk For Schizophrenia

Matcheri Keshavan¹, Jaya Padmanabhan¹, Neeraj Tandon¹, Jai Shah¹, Diana Mermon¹, Debra Montrose¹

¹Harvard Medical School, Boston, MA, USA, ²University of Pittsburgh, Pittsburgh, PA, USA

A substantial proportion of young relatives at high familial risk for Schizophrenia (FHRS) show premorbid cognitive, psychopathological and neurobiological alterations; Genetic and environmental factors interactively contribute to such risk. However we still do not have reliable predictors of later psychopathology in FHRS. We have previously reported that baseline measures of schizotypy and positive prodromal symptoms are highly predictive of later psychosis, and that the combined effect of multiple phenotypic variables including impaired cognition is better than individual predictors alone. In a longitudinal study of FHRS subjects followed up to 3 years we examined the predictors of conversion. We combined several environmental risk factors (including obstetric complications, childhood trauma, cannabis abuse, and season of birth), weighted by odds ratios of these measures in the literature to create a "poly-envirome" score (PES). We examined the value of PES in FHRS subjects (n = 92) with follow-up data up to 3 years. PES significantly predicted psychosis converters (n = 14) at follow up (p = 0.004). A model using PES had a higher model fit (Nagelkerke R² = 0.17) than models using individual risk factors (range: 0.031-0.148). Combining familial risk, multiple environmental risk factors and premorbid phenotypic signatures might help prediction of psychosis risk in FHRS and thereby facilitate early intervention efforts.

Question and Answer Period

Discussant: Patrick McGorry, M.D., Ph.D., Orygen, the National Centre of Excellence in Youth Mental Health, Centre for Youth Mental Health, University of Melbourne, Parkville, Australia

Symposium Session 19

Friday, October 21, 2:45–4:15 p.m., Washington B

Thinking Through a “Fog of Cannabis”: Cannabis Use and Cognition

Chair: Marta Di Forti¹, Co-Chair: Robin Murray²

Speakers: Tom Freeman, Giorgio Di Lorenzo, Laura Ferraro, Tiziana Rubino

¹*Social Genetic and Developmental Psychiatry, Institute of Psychiatry, King's College, London, UK,* ²*Institute of Psychiatry, Psychology & Neuroscience, Department of Psychosis Studies, King's College London, London, UK*

The association between cannabis use and increased psychosis has been consistently reported. Nevertheless, it remains a topic of discussion, which is the relationship between adolescence cannabis use affects cognitive function. We propose to present data from general population and clinical samples to provide clear evidence of the direction of the association between cannabis use and cognitive function and finally to explore animal model data to point at the underlying biology. Firstly, Tom Freeman, in a sample of healthy volunteers will show that cannabis containing high THC (Delta-9-Tetrahydrocannabinol), its main active ingredient, is associated with a greater severity of addiction. It was also rated as most strongly associated with memory impairment. Furthermore, Giorgio Di Lorenzo, will presents data from a sample of healthy adolescents, suggesting that deficits in working memory performance are strongly associated with current cannabis use particularly in individuals with schizotypal traits. Laura Ferraro, from a large case-control pan-European sample, will report that patients who present with their First Episode of Psychosis (FEP) and a history of cannabis use have higher IQ and better pre-morbid sociability (age 12 and 16 years) compared FEP who never used cannabis. Finally Tiziana Rubino in her animal model of adolescence exposure to THC shows that chronic THC treatment induces a different epigenetic picture in the adolescent brain in comparison to the adult one. These different responses indicate how exposure to cannabis use, during brain development, might induce long-lasting adverse effects on cognition.

Talk 1

Comparing Different Types of Cannabis on Cognition, Reward and Addiction

Tom Freeman^{1,2}

¹*IOPPN, KCL,* ²*Clinical Psychopharmacology Unit University College London, London, UK*

Cannabis is used by ~182 million people each year. This number may increase as legalisation of recreational and/or medical use proliferates. Some people are more vulnerable to its harmful effects than others: genetics, age of onset and frequency of use are all important factors. Another key issue is the type of cannabis used. The cannabis plant produces over 100 ‘cannabinoids’ and the two most abundant of these (delta-9-tetrahydrocannabinol, ‘THC’ and cannabidiol, ‘CBD’) can cause opposite effects on brain and behaviour. I will present data from three studies: a naturalistic design measuring THC and CBD in 134 peoples’ own cannabis, a controlled study comparing the acute effects of cannabis with THC, THC + CBD and placebo in 16 volunteers, and a cross-sectional study of 2514 people using different types of cannabis. Study 1 found that cannabis containing THC only robustly impaired verbal memory. By contrast, cannabis with the same level of THC (but also containing CBD) caused no impairment. In study 2, THC enhanced anticipation of reward (‘wanting’) but attenuated the neural correlates of reward delivery (‘liking’), an effect

that was blocked by CBD co-administration. Study 3 found that cannabis containing high THC and negligible CBD was associated with a greater severity of addiction. It was also rated as most strongly associated with memory impairment and paranoia. In conclusion, these findings add to accumulating evidence linking high-potency cannabis to users’ risk of psychosis. They further demonstrate that the type of cannabis used has critical implications for cognition and mental health.

Talk 2

Cannabis Use and Working Memory Deficits in a General Population Sample of Young Adults

Giorgio Di Lorenzo

Laboratory of Psychophysiology, Chair of Psychiatry, Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy, Psychiatry and Clinical Psychology Unit, Department of Neurosciences, Fondazione Policlinico “Tor Vergata”, Rome, Italy

Working memory (WM) is commonly impaired in people affected by schizophrenia and in those individuals at high-risk for psychosis. Information about WM in the general population exposed to risk factors for psychosis is sparse. The aim of the current study was to investigate, in a general population of young adults, the relation between the WM performance and the presence of risk factors for psychosis. In a large sample of young adults WM was measured with the Change Localization Task (CLT), along with the collection of information on past and current exposition to risk factors for psychosis (early traumatic life events, smoking, cannabis use). The schizotypal trait, another risk factor for psychosis, was also measured through the Schizotypal Personality Questionnaire (SPQ). Relations between WM and single risk factors for psychosis were not significant. When the population was divided based on the presence or the absence of a current use of cannabis relations between WM and other risk factors for psychosis emerged. In particular, in the current cannabis users, and not in the past cannabis users, higher scores of SPQ were associated with a worse WM performance. These findings revealed that deficits of WM in young adults are associated with schizotypal traits and current cannabis use. These results, moreover, suggest a speculative model about the role of cannabis use in determining WM alteration among subgroup with schizotypal features in the general population.

Talk 3

Better IQ but Worse Premorbid Academic Adjustment in Cannabis-Users Psychotic Patients Across Europe: Another Brick in the Intuition

Laura Ferraro¹, Veronica Cappuccio¹, Erika La Cascia¹, Lucia Sideli¹, Alice Mule¹, Fabio Seminero¹, Giada Tripoli¹, Robin Murray², Daniele La Barbera¹, Marta Di Forti²

¹Section of Psychiatry and Department of Statistics, Medical School, University of Palermo, Italy, ²IoPPN, King's College London, UK

Purpose: Several studies report that patients with psychosis who used cannabis in their lifetime have a better cognitive performance than those who did not and this association is most likely due to a better premorbid functioning. We aimed to test the hypothesis of a better premorbid functioning in First Episode Psychosis (FEP) cannabis-using and non-using patients coming from different European countries.

Materials and Methods: 1.745 people (746 cases; 999 healthy controls) completed the assessment for Intellectual Quotient (IQ) (WAIS-brief version) premorbid adjustment (Premorbid Adjustment Scale – PAS) and cannabis use (CEQ-Revised). We first obtained two main factors from PAS: “Premorbid Social Adjustment” (PSA) and “Premorbid Academic Adjustment” (PAA). We therefore performed linear mixed models with IQ, PSA, and PAA as dependent variables and cannabis lifetime (Yes/No) and subject status (Cases/Controls) as independent variables.

Results: across all countries, IQ was higher in cannabis users patients compared to non users ($p = 0.027$). Conversely, PAA resulted worst in cannabis-users patients than non users ($p < 0.001$). Nevertheless, cannabis-users patients showed better PSA scores than non users ($p = 0.009$) and this difference was significantly greater in patients than controls ($p = 0.038$). Moreover, a better IQ resulted related to a better PAA (<0.001) but not to PSA ($p = 0.260$).

Conclusions: a better IQ is not directly predictable by a better adjustment at school between 12 and 16 years (PAA), even if these two scores are positively correlated. Additionally, we can speculate an independent relationship of IQ and a better sociability between 12 and 16 years (PSA) with cannabis use.

Talk 4

Effects of Adolescent THC Exposure in the Prefrontal Cortex of Female Rats: From Histone Modifications to Cognitive Deficits

Tiziana Rubino, Pamela Prini, Federica Penna, Daniela Parolaro

DiSTA and Neuroscience Center, University of Insubria, Varese, Italy

The emerging role of epigenetics in the development of psychiatric diseases led us to hypothesize that epigenetic modifications could play a part. We investigated whether epigenetic mechanisms may contribute to the long-lasting adverse effects triggered by THC exposure in an experimental model represented by adolescent animals. We first performed a time-course study of different histone H3 modifications occurring in the prefrontal cortex (PFC) of female rats exposed to THC during adolescence. Next, to verify the vulnerability of the adolescent brain, we performed the same analysis after adult THC exposure. Finally, through the administration of a specific epigenetic drug, we investigated the role played by histone modifications in the complex phenotype present in adult animals after adolescent THC exposure. Adolescent THC exposure induced alterations in selective histone modifications in different cerebral areas relevant for cognition and emotionality. On the contrary, adult THC exposure induced histone modifications ending in transcription activation. Changes in histone modifications were more widespread and intense after adolescent treatment in comparison with that of adults, supporting the existence of higher adolescent sensitivity. Finally, pharmacological blockade of the enzyme responsible for the main histone modification induced by adolescent THC exposure during the THC

treatment was able to prevent THC-induced cognitive deficits at adulthood. As a whole these data suggest that chronic THC treatment induces a different epigenetic picture in the adolescent brain in comparison to the adult one. This different response might play a part in long-lasting adverse effects triggered by THC in adolescent animals.

Symposium Session 20

Friday, October 21, 2:45–4:15 p.m., Manzoni

New Models of Psychosocial Rehabilitation in Early Phases of Psychosis

Chair: Masafumi Mizuno¹, Co-Chair: Giancarlo Vinci²

Speakers: Takahiro Nemoto, Sung-Wan Kim, Raffaele Popolo, Andrea Fiorillo

¹Department of Neuropsychiatry, Toho University School of Medicine, Tokyo, Japan, ²Department of Mental Health Rome, Italy

Social functioning represents a crucial component of patients' quality of life. Therefore, interventions on patients affected by severe conditions should not only aim to the remission of symptoms but also to the improvement of such functions. Moreover, it is necessary to evaluate social functioning in the context of interpersonal relations, within the family and in the vocational sphere. This has the objective of designing psychosocial rehabilitation models, including both social functioning impairment and psychopathological picture treatment. In this symposium, we are going to discuss models that can inspire such designs. The focus will be on interventions that can improve the patients' social functioning and quality of life. We will present interventions on different functions. Firstly, cognitive functioning on acute phases of schizophrenia, secondly, metacognitive treatments based on group therapy with the use of smartphones as well as sport practice. Lastly, we will present a new psychoeducational approach to improve lifestyle behaviours.

Talk 1**Cognitive Rehabilitation in Acute Phase of Schizophrenia and Its Feasibility**

Takahiro Nemoto¹, Kiyoaki Takeshi¹, Miki Tobe¹, Hidehito Niimura², Ryosuke Ito³, Akiko Kojima¹, Megumi Iba¹, Tomoyuki Funatogawa¹, Taiju Yamaguchi¹, Naoyuki Katagiri¹, Naohisa Tsujino¹, Masafumi Mizuno¹

¹Toho University School of Medicine, Tokyo, Japan, ²Keio University School of Medicine, Tokyo, Japan, ³Funabashi Special Support Education School, Chiba

Although rehabilitation in psychiatry is usually implemented in chronic phase, the importance of rehabilitation in acute phase is emphasized in the field of physical medicine. Psychiatric rehabilitation in acute phase includes a number of problems to be resolved like psychiatric symptoms and lack of spontaneity. The aims of the present study were to examine the feasibility and the effectiveness of cognitive rehabilitation in acute phase of schizophrenia. In-patients with schizophrenia aged 15 to 50 years who were admitted to the Toho University Omori Medical Center in Tokyo were recruited for this study. Patients who could start cognitive rehabilitation within 2 weeks from the admission were considered to be candidates for this study. We developed a cognitive rehabilitation program that consisted of an 8-week workbook that was suitable to patients in acute phase. Eighty-three in-patients with schizophrenia were newly admitted to the hospital in 15 months. After screening by exclusion criteria, 49 patients were considered introducing into the study. Of them, 22 patients (45%) agreed to their participation and started the cognitive rehabilitation program. Their mean GAF score was 32 and the mean period between the admission and the start of the program was 9 days. Sixteen patients (73%) completed the program. Their GAF score was significantly improved and their satisfaction with the program was good. Conclusion: About half of patients with schizophrenia could start cognitive rehabilitation and their continuation was good even in acute phase in which various psychotic symptoms and disabilities were obvious.

Talk 2**Group Cognitive-Behavioural Therapy and Smartphone Application for Young Individuals with Early Psychosis**

Sung-Wan Kim

Chonnam National University Hospital, Gwangju, South Korea; Gwangju Bukgu Community Mental Health Center, South Korea

This study aimed to develop group cognitive-behavioural therapy (CBT) and the Smartphone application for case management of young individuals with early psychosis. Methods: We developed a Korean version of group CBT consisting of metacognitive training, cognitive restructuring, life style modification, and stress management. The Subjective Wellbeing under Neuroleptics (SWN-K) scale, Ambiguous Intentions Hostility Questionnaire (AIHQ), Drug Attitude Inventory (DAI), Beck Depression Inventory (BDI), and Perceived Stress Scale (PSS) were administered before and after 14 sessions. In addition, we developed and launched a Smartphone app for cognitive-behavioural case management and symptom monitoring. A total of 34 patients completed scales both before and after group CBT. Scores on the SWN and DAI increased significantly (p -value = 0.044 and < 0.001 , respectively) and those on the AIHQ and PSS decreased significantly (p -value = 0.005 and 0.045) after group CBT. More than 80% of participants using the app reported that it was easy to learn to use it, and no one described this app as very complicated. About 80% of participants were satisfied with this app, and 70% reported that they received help as a result of using this app. Group CBT had a positive effect on the quality of life, attitude toward treatment, perceived stress, and suspiciousness of patients with early psychosis. Furthermore, a Smartphone app for case management may be useful for

young individuals with early psychosis. This study may contribute to the development of a youth- and customer-friendly case management system for individuals with early psychosis.

Talk 3**The Metacognitive-Interpersonal Model in Psychosocial Rehabilitation**

Raffaele Popolo¹, Giancarlo Vinci², Maurizio Parisi³, Bruno Ruscello³, Francesca R. Vinci⁴, Andrea Balbi²

¹Centro Terapia Metacognitiva Interpersonale Rome, Italy, ²Department of Mental Health Rome, Italy, ³University of Rome Tor Vergata, Italy, ⁴University of Nottingham, UK

Numerous studies have shown the presence in schizophrenic patients of impaired metacognitive functions, i.e. those skills that enable awareness of mental status. We designed a model of psychological rehabilitation with the aim to improve metacognitive functioning, testing the hypothesis that an early intervention can favour a more rapid recovery of the compromised abilities. We evaluated the variation of such functions in patients who took part in a psychosocial rehabilitation programme, using an integrated model of intervention. This consisted in a group sport activity of 120 minutes twice a week, followed by a metacognitive psychotherapeutic group session of 90 minutes once a week. Two groups of patients with diagnoses within the schizophrenia spectrum were compared. All subjects were selected among the patients of the Department of Mental Health Rome 3. The first group was made up of 21 subjects, aged between 18 and 25, whilst the second involved 16 patients, between 26 and 35 years of age. We performed formal assessments at the baseline and after one year of intervention, running a battery of metacognitive tests specifically constructed by our research team. These included the Hinting Task, the Brune sequencing pictures task, BCSI and the Eyes tests. As for psychopathological scales, we performed the PANSS and Cgi test, while we chose Gaf as a function test and SF36 as a quality of life assessment tool. Preliminary results confirmed the impairment of metacognitive functions in both samples. We expect that further results will support our hypothesis, especially in young subjects.

Talk 4

A New Psychoeducational Approach to Improve Lifestyle Behaviours in Patients with Severe Mental Disorders

Andrea Fiorillo, Mario Luciano, Gaia Sampogna, Valeria Del Vecchio
University of Naples, SUN, Italy

People with severe mental illness (SMI) have an increased rate of chronic physical illnesses and an unacceptable reduced life expectancy of up to 30 years compared to the general population. In particular, a higher prevalence of cardiovascular diseases, diabetes, obesity, metabolic syndrome, cancer and infectious diseases has been found in these patients. The higher mortality rates can be explained by several factors including unhealthy lifestyle, disparities in access and quality of health care, and side effects of antipsychotics. As regards lifestyle behaviours, patients with SMI are more frequently heavy smokers with a low level of physical activity, unhealthy eating habits and abuse of alcohol or drug. Most clinical guidelines for the treatment of SMI suggest the use of these interventions and emphasize the need of regular health monitoring and check-ups. Lifestyle behaviours can be improved through specific psychosocial interventions. Recently several psychosocial interventions, such as the STRIDE and the CHANGE trials, have been developed with a specific focus on lifestyle modifications. These approaches have been proved to be effective in improving patients' physical health indices, such as BMI, waist circumferences, weight, blood pressure and cardiovascular risk index. We developed a new psychoeducational group intervention for improving lifestyle behaviours in patients with SMI. Our approach, which includes elements of classical psychoeducation, motivational interview, problem solving and health coaching techniques, addresses: healthy eating, smoking cessation, physical activity, sleep-wake cycle, sexual habits, alcohol abuse. Sessions take place on a weekly basis for a period of six months (24 sessions in total). Each session lasts about 90 minutes and includes: a) information on the topic of the session; b) motivation to change; c) group discussion; d) physical activity.

Question and Answer Period

Discussant: Giancarlo Vinci, *Department of Mental Health, Rome, Italy*

Symposium Session 21

Friday, October 21, 2:45–4:15 p.m., Foscolo

Results of New Intervention Trials in People at Clinical High Risk of Psychosis

Chair: Patrick D. McGorry M.D., Ph.D.,^{1,2}, Co-Chair: Andreas Bechdolf³

Speakers: Helen J. Stain, Mark van der Gaag, Andreas Bechdolf, Patrick D. McGorry

¹Orygen, the National Centre of Excellence in Youth Mental Health, Parkville, Australia ²Centre for Youth Mental Health, University of Melbourne, Parkville, Australia, ³Department of Psychiatry, Psychotherapy and Psychosomatics, Vivantes Hospital am Urban and Friedrichshain, Charite Medicine Berlin, Germany

Recent research has indicated that preventative intervention is likely to benefit patients at clinical high risk (CHR) for psychosis, both in terms of symptom reduction and delay or prevention of onset of threshold psychotic disorder. However a number of questions regarding the long term effects and the differential effects of preventive interventions are still open. In this symposium on actual randomized controlled trials (RCT) some of these issues will be addressed. Stain et al., present results of a RCT comparing CBT with Non Directive

Reflective Listening (NDRL) in addition to standard care in 57 young adults with CHR, indicating that in this group there were no differences between the treatment groups in terms of transitions to psychosis and functioning. Van der Gaag et al present results of a RCT comparing CBT and Tau with TAU alone, which indicated an effect on CBT on transitions still at 4 year follow-up in $n = 113$. Bechdolf et al., compared CBT, with Clinical management and placebo and clinical management and aripipazole in more than 200 participants with CHR. The results indicated that CBT presents with lowest progression rates towards psychosis on a descriptive level, although only on a trend level when compared with clinical management and placebo. McGorry et al., will present data from a large 6-months, double-blind, placebo controlled RCT of 1.4 g day⁻¹ omega-3 polyunsaturated fatty acids in CHR patients, in order to a replication the large effects of an earlier small scale trial.

Talk 1

A Randomised Controlled Trial of Cognitive Behaviour Therapy Versus Non-Directive Reflective Listening for Young People at Risk of Developing Psychosis

Helen J. Stain¹, Sandra Bucci², Amanda L. Baker³, Vaughan Carr⁴, Richard Emsley⁷, Sean Halpin⁸, Terry Lewin³, Ulrich Schall^{5,9,10}, Vanessa Clarke³, Kylie Crittenden¹¹, Mike Startup⁸

¹School of Medicine, Pharmacy and Health, Durham University, UK, ²School of Psychological Sciences, University of Manchester, Manchester, UK, ³School of Medicine and Public Health, University of Newcastle, NSW, Australia, ⁴School of Psychiatry, University of New South Wales, NSW, Australia, ⁵Schizophrenia Research Institute, NSW, Australia, ⁶Department of Psychiatry, Monash University, Vic, Australia, ⁷Institute of Population Health, University of Manchester, Manchester, UK, ⁸School of Psychology, University of Newcastle, NSW, Australia, ⁹Priority Centre for Translational Neuroscience & Mental Health Research, University of Newcastle, NSW, Australia, ¹⁰Hunter Medical Research Institute, NSW, Australia, ¹¹Western New South Wales Local Health District, NSW, Australia

Background Intervention trials for young people clinically at risk (AR) for psychosis have shown cognitive behaviour therapy (CBT) to have promising effects on treating psychotic symptoms but have not focused on functional outcomes. We hypothesised that compared to an active control, CBT would: (i) reduce the likelihood of, and/or delay, transition to psychosis; and (ii) reduce symptom severity while improving social functioning and quality of life, whether or not transition occurred. Method This was a single-blind randomised controlled trial for young people AR for psychosis (aged 14-35 years) comparing CBT to Non Directive Reflective Listening (NDRL) in addition to standard care, with a 6 month treatment phase and 12 months of follow-up. Results There were 57 young people (mean age of 16.5 years) randomised for treatment. The rate of transition to psychosis was 5%, with all 3 transitions occurring in the CBT condition (baseline, 2 months and 5 months respectively). The active control condition, NDRL, resulted in a significantly greater reduction in distress associated with psychotic symptoms compared to CBT. Both conditions showed reductions in the frequency and intensity of psychotic symptoms over time. There were no significant treatment effects on global, social or role functioning. Conclusion Our sample was higher functioning, younger and experiencing lower levels of psychotic like experiences than other trials. The significantly better treatment effect of NDRL on distress associated with psychotic symptoms supports the recommendations for a stepped-care model of service delivery. This treatment approach would accommodate the younger AR population and facilitate timely intervention.

Talk 2

The Four-Year Follow-Up Data of Cognitive Behavioural Therapy for Ultra High Risk Subjects

Mark van der Gaag^{1,2}, Helga K. Ising¹, Tamar C. Kraan³, Judith Rietdijk¹, Sara Dragt³, Rianne M. C. Klaassen⁴, Nynke Boonstra⁵, Dorien H. Nieman², Monique Willebrands-Mendrik³, David P. DG. van den Berg¹, Wim Veling⁶, Filip Smit^{2,7,8}

¹Parnassia Psychiatric Institute, The Hague, The Netherlands, ²VU University and EMGO Institute for Health and Care Research, Amsterdam, The Netherlands, ³Academic Medical Center, Amsterdam, The Netherlands, ⁴De Bascule, Academic Center for Child and Adolescent Psychiatry, Amsterdam, The Netherlands, ⁵Friesland Mental Health Services, Leeuwarden, The Netherlands, ⁶University Medical Center Groningen and University of Groningen, Groningen, The Netherlands, ⁷Trimbos Institute (Netherlands Institute of Mental Health and Addiction), Utrecht, The Netherlands, ⁸VU University Medical Center, Amsterdam, The Netherlands

Previously, we demonstrated that cognitive behaviour therapy for ultra-high risk (called CBTuhr) halved the incidence of psychosis over an 18-month period. The four-year follow-up was conducted. Of the 196 patients included in the study, 113 consented to a 4-year follow-up (57.7%; CBTuhr = 56 vs TAU = 57). Over the follow-up period, the number of participants in the CBTuhr group making the transition to psychosis increased from 10 at 18-month follow-up to 12 at 4-year follow-up, whereas it did not change in the TAU group ($n = 22$); this still represents a clinically important (incidence rate ratio [IRR] = 12/22 = 0.55) and significant effect ($F(1,5) = 8.09$, $P = .03$), favouring CBTuhr. The odds ratio of CBTuhr compared to TAU was 0.44 (95% CI: 0.24-0.82) and the number needed to treat was 8. Moreover, significantly more patients remitted from their UHR status in the CBTuhr group (76.3%) compared with the TAU group (58.7%) [$t(120) = 2.08$, $P = .04$]. Transition to psychosis was associated with more severe psychopathology and social functioning at 4-year follow-up. CBTuhr to prevent a first episode of psychosis in persons at UHR of developing psychosis is still effective at 4-year follow-up. Our data also show that individuals meeting the formal criteria of a psychotic disorder have worse functional and social outcomes compared with non-transitioned cases.

Talk 3

PREVENT: A Randomized Controlled Trial Comparing Cognitive Behavioural Therapy, Clinical Management and Aripiprazole and Clinical Management and Placebo for the Prevention of First Episode Psychosis

Andreas Bechdolf^{1,2}, Hendrik Mueller¹, Wolfgang Gaebel⁴, Alkomiet Hasan⁵, Wolfgang Maier⁸, Georg Juckel⁶, Martin Lambert⁷, Marion Lautenschlager³, Franziska Rausch¹⁰, Michael Riedel¹¹, Frank Schneider⁹, Joachim Klosterkötter¹

¹Department of Psychiatry and Psychotherapy, University of Cologne, Germany, ²Vivantes Hospital am Urban/Charité University Medicine, Berlin, Germany, ³Charité University Medicine Berlin, ⁴Heinrich-Heine-University Düsseldorf, Germany, ⁵Georg-August-University Göttingen, Germany, ⁶Ruhr University Bochum, Germany, ⁷University Medical Centre Hamburg-Eppendorf, Germany, ⁸Friedrich Wilhelms University of Bonn, Germany, ⁹RWTH Aachen, ¹⁰Central Institute of Mental Health Mannheim, Germany, ¹¹Ludwig-Maximilians-University Munich, Germany

Purpose: Antipsychotics, omega-3-fatty acids and psychotherapy have been found to be effective to prevent transition to first episode psychosis in individuals at clinical high risk for psychosis (CHR). However, little data is available regarding the differential effects of the preventive interventions. PREVENT was a multicenter, prospective, randomized, blinded trial with three parallel groups designed to compare 1. Aripiprazole (ARI) + clinical management (CM) and 2. cognitive behavioural therapy (CBT) to 3. placebo (PL) + clinical management.

Materials and Methods: Individuals aged 18-49 identified as CHR by UHR and/or basic symptoms COGDIS criteria were assessed at baseline, 28 and 52 weeks including clinical symptoms, social functioning, quality of life and safety. The primary outcome was progression and the secondary was transition to psychosis.

Results: Overall 280 individuals [mean age 24.4 (5.1) years; about 66 % male] were randomized. In terms of the primary outcome, there was no statistical difference between the three treatment arms ($p > 0.05$). Exploratory pairwise comparisons showed a statistical trend in favour of CBT compared with CM + PL. With respect to the secondary outcome, there was a reduction in favour of CBT compared to CM + ARI also approaching statistical significance. Drop-out rates between the arms differed over time ($p < .05$), with indications for more premature terminations in ARI + CM and PL + CM compared to CBT.

Conclusions: Pairwise comparisons showed a clinically relevant reduction regarding the primary (about 35 %) and secondary outcome (about 40 %) in favour of CBT. Lower drop-out rates in CBT could be interpreted as higher adherence and acceptance of psychotherapy within this trial.

Talk 4

NEURAPRO-E: A Multicentre Randomized Controlled Trial of Omega-3 Fatty Acids and Cognitive-Behavioural Case Management for Patients at Ultra High Risk of Schizophrenia and Other Psychotic Disorders

Patrick D. McGorry¹, B Nelson¹, C Markulev¹, A R Yung², G Berger³, L de Haan⁴, A Riecher-Rössler⁵, M Nordentoft⁶, E Y Chen⁷, S Verma⁸, Ian Hickie⁹, G P Amminger¹

¹Orygen, the National Centre of Excellence in Youth Mental Health, Centre for Youth Mental Health, University of Melbourne, Parkville, Australia, ²Institute of Brain, Behaviour and Mental Health, University of Manchester, Manchester, UK, ³Department of Child and Adolescent Psychiatry, University of Zurich, Zurich, Switzerland, ⁴Academic Psychiatric Centre, AMC, Amsterdam, The Netherlands, ⁵Psychiatric University Clinics, University Psychiatric Outpatient Department, Basel, Switzerland, ⁶Department of Psychiatry E, Bispebjerg Hospital, Copenhagen, Denmark, ⁷Department of Psychiatry, University of Hong Kong, Hong Kong, ⁸Early Psychosis Intervention, Institute of Mental Health, Singapore, ⁹Brain & Mind Research Institute, University of Sydney, NSW, Australia

Aim: Recent research has indicated that preventative intervention is likely to benefit patients 'at-risk' for psychosis, both in terms of symptom reduction and delay or prevention of onset of threshold psychotic disorder. The strong preliminary results for the effectiveness of omega-3 polyunsaturated fatty acids (PUFAs), coupled with the falling transition rate in ultra high-risk (UHR) samples, mean that further study of such benign, potentially neuroprotective interventions is clinically and ethically required. Employing a multicentre approach, enabling a large sample size, this study will provide important information with regard to the use of omega-3 PUFAs in the UHR group.

Methods: This trial is a 6-month, double-blind, randomized placebo-controlled trial of 1.4 g day⁻¹ omega-3 PUFAs in UHR patients aged between 13 and 40 years. The primary hypothesis is that UHR patients receiving omega-3 PUFAs plus cognitive-behavioural case management (CBCM) will be less likely to transition to psychosis over a 6-month period compared to treatment with placebo plus CBCM. Secondary outcomes will examine symptomatic and functional changes, as well as examine if candidate risk factors predict response to omega-3 PUFA treatment in the UHR group.

Conclusion: This is the protocol of the NeuraproE study. Utilizing a large sample, results from this study will be important in informing indicated prevention strategies for schizophrenia and other psychotic disorders, which may be the strongest avenue for reducing the burden, stigmatization, disability and economic consequences of these disorders.

Question and Answer Period

Discussant: Alison Yung, Institute of Brain, Behavior and Mental Health, University of Manchester, UK

Symposium Session 22

Friday, October 21, 4:30–6:00 p.m., Washington A

Pharmacological and Non-Pharmacological Interventions to Reduce Cardiometabolic Risk During Treatment of Mental illness: Managing the Risks of Early Intervention

Chair: Ane Storch Jakobsen¹

Speakers: John W Newcomer, Jackie Curtis, Ane Storch Jakobsen, Faith Dickerson

¹University of Copenhagen, Mental Health Center Copenhagen, Denmark

Early intervention for mental health disorders offers the potential for important advantages in managing long term mental health outcomes. Importantly, major mental health conditions are also associated with an increased risk for diabetes and cardiovascular disease compared with the general population, largely explained by increased rates of key risk factors like overweight and obesity, dyslipidaemia, hyperglycaemia, hypertension, and smoking. While genetic influences and disease-related lifestyle factors have been implicated as contributors to overall risk, unmedicated first episode patients have been observed to have cardiometabolic risk similar to the general population, with treatments such as antipsychotic medication associated with substantial increases in risk factors for both diabetes and cardiovascular disease. Recent research and international guidelines have focused on opportunities to increase screening and monitoring of risk during treatment, but the effect of pharmacological and non-pharmacological treatments to mitigate cardiometabolic risk –especially early in treatment– have received limited study. This symposium will review evidence that early pharmacological treatment of mental health conditions can be associated with rapid onset adverse effects on long-term risk for cardiovascular disease and diabetes, and then report on the results of a series of important studies of pharmacological and non-pharmacological interventions to reduce cardiometabolic risk in patients with mental health disorders. The mixed results of these studies indicate the importance of avoiding high-risk pharmacotherapies in the treatment of mental illness and the high-value of early screening and intervention to manage the medical health outcomes of patients with mental health disorders.

Talk 1

Rapid Onset Adverse Cardiometabolic Effects of Pharmacotherapy for Mental Health Disorders: Review of the Evidence Including Results from the NIMH-funded Metabolic Effects of Antipsychotics in Children (MEAC) Study

John W Newcomer¹, Ginger E Nicol²

¹Charles E. Schmidt College of Medicine, Florida Atlantic University, USA, ²Washington University School of Medicine, St. Louis, MI USA

Antipsychotic and other psychotropic treatments are associated with adverse effects on body weight and other risk factors for diabetes and cardiovascular disease. Evidence from observational databases suggest rapid onset risk for diabetes and dyslipidaemia. Randomized clinical trials have rarely been designed and powered to measure metabolic risk as primary endpoints. The randomized, NIMH-funded Metabolic Effects of Antipsychotics in Children study (MEAC) characterized the metabolic effects of 12 weeks of antipsychotic treatment using gold-standard measures in children with disruptive behaviours. Antipsychotic-naïve youth with clinically significant aggression/irritability were randomized to treatment with aripiprazole, olanzapine or risperidone. Over just 12 weeks, the pooled patient sample increased the rate of overweight and obesity from a

US paediatric general population norm of 30% to a remarkable 47%. Significant effects of treatment were observed on measures of adiposity (body fat) and insulin sensitivity. Differential effects of individual treatments were observed on measures of adiposity, insulin sensitivity and other endpoints. Importantly, treatment resulted in marked improvement in irritability/aggression, with no significant differences across individual treatments. The results indicate that antipsychotic treatment of previously antipsychotic-naïve children results in rapid onset adverse effects on metabolic risk. While risk differs significantly across individual treatments, the efficacy of the treatments was similar, suggesting the importance of careful selection of pharmacotherapies to minimize risk and improve overall effectiveness. The results suggest that antipsychotics should be used judiciously and with careful metabolic monitoring, and underscore the importance of adjunctive pharmacological and non-pharmacological treatments to manage cardiometabolic risk in patients who require psychotropic therapy.

Talk 2

Keeping the Body in Mind for Youth Experiencing Psychosis: Translating Research into Routine Practice

Jackie Curtis^{1,2}, Andrew Watkins², Scott Teasdale², Oscar Lederman², Megan Kalucy^{1,2}, Julia Lappin^{1,2}, Katherine Samaras¹, Simon Rosenbaum¹, Philip Ward¹

¹University of New South Wales, Sydney, Australia, ²South Eastern Sydney Local Health District, Sydney, Australia

The Bondi “Keeping the Body in Mind” (KBIM) program is a multidisciplinary, 12-week intervention aimed at attenuating weight gain in young people (15–25 years) recently commenced on antipsychotic medication (within 4 weeks). KBIM includes weekly, individualized, and group-based dietetic, exercise, health-coaching and motivational interviewing components delivered by specialist clinicians. In addition, peer-wellness coaches encourage participation and adherence. Participants who completed KBIM ($n = 16$) experienced significantly less weight gain than a comparison group ($n = 12$) who received best-practice FEP care without additional lifestyle intervention elements. There was no change in waist circumference in the intervention group, whilst waist circumference increased significantly for controls. Seventy-five percent (75%) of the intervention group did not experience clinically significant weight gain. Two-year follow up data for the intervention group ($n = 13$) indicated that preventing weight and waist circumference gains can be sustained when participants continue to have access to key lifestyle intervention elements (gym, cooking group, sports group). Primary outcomes from the 12-week program have been replicated in a second sample of youth with FEP ($n = 17$). KBIM is now being extended to other adults with SMI. Multidisciplinary early lifestyle interventions can attenuate antipsychotic induced weight gain in young people with FEP and may be an important means of achieving the key Healthy Active Lives (HeAL) targets (www.iphys.org.au). Additional components of the program now include oral health and sexual health screening. People with psychosis deserve support to secure the same life expectancy and expectations of life as their peers who do not have psychosis.

Talk 3

A Randomized Clinical Trial Investigating the Effect of a Lifestyle Coaching Intervention on Cardiovascular Risk in People with Schizophrenia and Overweight

Ane Storch Jakobsen^{1,2}, Helene Speyer^{1,2}, Hans Christian N Brix³, Merete Nordentoft^{1,2}

¹Mental Health Center Copenhagen, Denmark, ²University of Copenhagen, Denmark, ³Aarhus University Hospital, Mental Health Center Aarhus, Denmark

CHANGE is a randomized, parallel-group, superiority, multi-centre trial with blinded outcome assessment, testing the efficacy of an intervention aimed to improve cardiovascular risk profile and hereby potentially reduce mortality. A total of 428 patients with schizophrenia spectrum disorders and abdominal obesity were recruited and centrally randomized 1:1:1 to 12 months of lifestyle coaching plus care coordination plus treatment as usual (N = 138), or care coordination plus treatment as usual (N = 142), or treatment as usual alone (N = 148). The primary outcome was 10-year risk of cardiovascular disease assessed post-treatment and standardized to age 60 using the Copenhagen risk score, which is a composite measure including both non-modifiable (gender, family history of cardiovascular disease, prior heart disease) and modifiable factors (smoking, diabetes mellitus, total cholesterol, high density lipoprotein (HDL) cholesterol, systolic blood pressure, and body mass index). At 12 months follow-up, the mean 10-year risk of cardiovascular disease was $8.4 \pm 6.7\%$ in the group receiving lifestyle coaching, $8.5 \pm 7.5\%$ in the care coordination group, and $8.0 \pm 6.5\%$ in the treatment as usual group ($p = 0.41$). We found no intervention effects for any secondary or exploratory outcomes, including cardiorespiratory fitness, physical activity, weight, diet and smoking. In conclusion, the CHANGE trial did not support superiority of individual lifestyle coaching or care coordination compared to treatment as usual in reducing cardiovascular risk in patients with schizophrenia spectrum disorders and abdominal obesity. At the symposium we will be able to present and discuss the 2 years follow-up results

Talk 4

Comprehensive Cardiovascular Risk Reduction Trial (IDEAL Trial) in Persons with Serious Mental Illness: Description and Baseline Results

Faith Dickerson¹, Arlene Dalcin², Gerald Jerome³, Nae-Yuh Wang², Deborah Young⁴, Lawrence Appel², Joseph Gennusa², Stacy Goldsholl², Ann Heller², Courtney Cook², Gail L Daumit²

¹Sheppard Pratt Health System, Maryland, USA, ²Johns Hopkins University School of Medicine, Maryland, USA, ³Towson University, Maryland, USA, ⁴Kaiser Permanente Research, CA, USA

Purpose: Persons with serious mental illness (SMI) have an extraordinary burden of cardiovascular disease risk factors. We describe baseline data and intervention strategies for an ongoing NIH-funded trial of an 18-month comprehensive cardiovascular risk reduction program.

Materials and Methods: The IDEAL Trial will enrol 250 adults with SMI with at least one cardiovascular risk factor from 4 psychiatric rehabilitation program and clinic sites of a large community mental health organization in Maryland. As the control condition, we provide group exercise classes and healthy menu changes for all sites. Individuals randomized to active intervention in addition receive: individual cardiovascular risk reduction counselling (e.g., smoking cessation, weight management) by a health coach, a mental health organization employee; and 2) a study nurse who communicates/coordinates with primary care providers to advocate for optimal management of health risk factors (e.g., lipid, blood pressure and diabetes control).

Results: Of the 193 enrolled to-date, 55% are female, and 36% are African-American with mean age of 49 (SD 12) years. At baseline, 37% have diabetes, 44% have hypertension and 50% smoke, with

mean Framingham global risk score of 12.1% (SD 11.6). We will describe detailed intervention elements including prioritization and management of multiple risk factors in a population with high baseline risk for cardiovascular disease.

Conclusion: Evidence-based approaches to reduce cardiovascular disease risk in those with SMI are urgently needed. This randomized clinical trial will provide a rigorous evaluation of a practical intervention designed to improve cardiovascular health in this population.

Question and Answer Period

Discussant: John W Newcomer, Charles E. Schmidt College of Medicine Florida Atlantic University, Boca Raton, FL, USA

Symposium Session 23 Friday, October 21, 4:30–6:00 p.m., Washington B

Symptomatic and Neurobiological Characteristics of Clinical High Risk States of Psychosis

Chair: Chantal Michel¹, Co-Chair: Anastasia Theodoridou²

Speakers: Chantal Michel, Anastasia Theodoridou, Jochen Kindler, Diana Wotruba

¹University Hospital of Child and Adolescent Psychiatry and Psychotherapy, Bern, Switzerland, ²The Zurich Program for Sustainable Development of Mental Health Services (ZInEP); Department of Psychiatry, Psychotherapy and Psychosomatics, University Hospital of Psychiatry, Zurich, Switzerland

In clinical samples of specialized early detection and intervention services, both ultra-high risk (UHR) and basic symptom criteria are not only associated with a 1-year conversion rate of roughly 20% but also with various other impairments. Thus, in addition to symptoms included in clinical high risk (CHR) criteria, neurobiological predictors have been suggested to enhance predictive accuracy of CHR criteria. In the symposium different psychopathological and neurobiological aspects in CHR samples are presented: (1) neurocognitive characteristics of a sample of children and adolescents with and without a CHR state, (2) findings on differential subtle, self-experienced cognitive disturbances of a CHR-sample for psychosis, (3) results of an arterial spin labelling MRI study in 8-40-year old patients of the Bern Early Recognition and Intervention Centre, and (4) aberrations in dynamic-functional networks in a 16-35-year-old CHR of psychosis sample. Consistently, UHR criteria were assessed with the Structured Interview for Psychosis-Risk Syndromes (SIPS) and basic symptom criteria with the Schizophrenia Proneness Instrument, Adult (SPI-A) and Child and Youth version (SPI-CY), respectively. Study results and their comparison will shed light on clinical and neurobiological characteristics of CHR criteria and symptoms and the context in which these might occur.

Talk 1

Neurocognitive Deficits According to Norms in Adolescents With and Without Clinical High Risk States of Psychosis

Chantal Michel¹, Liz Rietschel¹, Nina Schnyder¹, Petra Walger², Maurizia Francini³, Benno G. Schimmelmann¹, Frauke Schultze-Lutter¹

¹University Hospital of Child and Adolescent Psychiatry and Psychotherapy, Bern, Switzerland, ²University Hospital of Child and Adolescent Psychiatry and Psychotherapy, Cologne, Germany,

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In the early detection of psychosis, neurocognitive predictors have been suggested to enhance predictive accuracy of clinical high risk (CHR) criteria. While mainly sample-dependent means of adult samples were used so far, a recent study of an adult sample used neurocognitive deficits defined according to test norms in order to facilitate individual prediction. Yet, data on child and adolescent samples are missing. We investigated the discriminative power of neurocognitive deficits defined according to norms in 8-17-year-olds. 84 CHR outpatients (AtRisk; mean age = 15.02 ± 2.20 , 39% male), 134 non-psychotic inpatients (ClinS; mean age = 14.46 ± 2.43 , 38% male) and 124 subjects of a general population sample (GPS; mean age = 13.91 ± 2.78 , 48% male) had been assessed with a neurocognitive battery, including a verbal fluency (VF) test, the Digit-Symbol Test, TMT A and B, the Auditory Verbal Learning Test (AVLT) and the Subject Ordered Pointing Task. GPS were slightly younger than AtRisk and ClinS ($\chi^2(2) = 7.656$, $p = 0.022$); no differences were found with regard to gender and premorbid IQ. Compared to ClinS and GPS, AtRisk more frequently exhibited deficits according to norms in verbal memory (AVLT learning capacity; 22.4% vs. 10.7%; OR = 2.4, 95% CI: 1.3-4.6) and VF (48.8% vs. 34.1%; OR = 1.8, 95% CI: 1.1-3.0), while ClinS and GPS did not differ. Partly in line with findings from adult samples, deficits in verbal memory and VF might be specifically associated with a CHR state in children and adolescents – even when compared to a more severely ill inpatient group. Yet, these findings need further examination in larger samples and longitudinal studies.

Talk 2

Perspectives on Subjective and Objective Cognitive Disturbances in the Clinical High Risk State for Psychosis

Anastasia Theodoridou^{1,2}, Mario Müller^{1,2}, Diane Dvorsky^{1,2}, Karsten Heekeren^{1,2}, Wulf Rössler^{1,3}

¹University Hospital of Psychiatry Zurich, The Zurich Program for Sustainable Development of Mental Health Services (ZInEP), Switzerland,

²Department of Psychiatry, Psychotherapy and Psychosomatics, University Hospital of Psychiatry, Zurich, Switzerland, ³Laboratory of Neuroscience (LIM-27), Institute of Psychiatry, University of Sao Paulo, Sao Paulo, Brazil

The clinical high risk (CHR) states for developing psychosis are well established and there is some evidence for neurocognitive deficits already in the prepsychotic period. The purpose of this study was to compare the subjective perception of cognitive disturbances in CHR individuals and objective variables according to neurocognitive measures. For the current study, we targeted individuals meeting criteria for a CHR state (either basic symptom criteria according to the Schizophrenia Proneness Instruments: SPI-A/SPI-CY, or ultra high-risk criteria according to the Structured Interview for Psychosis-Risk Syndromes). We examined the relationship of the “cognitive-attentional impediments” (CAI) and “cognitive disturbances” (CD) items from the SPI-A/SPI-CY with performance on neurocognitive tests. N = 221 participants have fully completed the baseline examinations. Using a latent class approach we empirically derived

homogeneous subgroups that showed unique patterns of CAI and CD. Based on a three-class solution, a “low thought initiative level” (LTI) subgroup and a “low functioning in receptive speech” (LRS) subgroup was found. In subsequent regression models LTI was linked to performance in verbal working memory and with perseveration-errors of the Wisconsin Card Test. The four-class solution derived another subgroup, “slowed down thinking” (SDT). SDT was associated with verbal fluency, Trail Making Test and FAIR. Our findings suggest differential subjective perceptions of neurocognitive functioning that can be subdivided into impaired thought initiative and disturbances of receptive speech. Specific associations with neurocognitive variables support this view. This raises the question of whether there are distinctive impaired subtypes as indicated by specific psychopathological and functional outcomes.

Talk 3

Cerebral Blood Flow in Psychosis Risk, First Episode Psychosis and Schizophrenia

Jochen Kindler¹, Frauke Schultze-Lutter¹, Daniela Hubl²

¹University Hospital of Child and Adolescent Psychiatry and Psychotherapy, Bern, Switzerland, ²University Hospital of Psychiatry and Psychotherapy, University of Bern, Switzerland

Research on clinical high risk (CHR) states for psychosis indicates increased presynaptic striatal dopamine synthesis in CHR individuals as compared to controls. An increase in metabolic rate might also affect cerebral blood flow (CBF). Here, we examined if CBF in striatum differs between patients with CHR, first episode psychosis (FEP) and schizophrenia (SZ) when compared with controls. A total of 59 patients of the Bern Early Recognition and Intervention Centre were included. A CHR state was met by 29 patients, 12 patients met criteria for FEP. The clinical controls (CC, n = 18) did not fulfil CHR criteria or suffered from psychosis. Ultra-High Risk criteria were assessed by the Structured Interview for Psychosis-Risk Syndromes, Basic Symptom criteria by the Schizophrenia Proneness Instrument. Additionally, patients with an ICD-10 diagnosis of schizophrenia (n = 32) and healthy controls (HC, n = 31), were included. A pseudo-continuous arterial spin labelling MR technique was used to measure CBF. Significantly increased CBF in the right striatum ($p < 0.05$, FWE corrected) was revealed in CHR and FEP as compared to CC. In comparison to HC, SZ demonstrated a significantly increased striatal CBF, in the caudate head and body ($p < 0.05$, FWE corrected). CBF in striatum correlated with positive symptom scores ($p < 0.001$) and executive dysfunctions ($p < 0.05$) in CHR. This is the first study to demonstrate increased neuronal activity within the striatum in CHR, FEP and SZ as compared to the respective controls. Our results indicate that increased CBF in striatum is a trait biomarker for psychosis risk, first episode psychosis and chronic schizophrenia.

Talk 4

Resting-State fMRI Dynamics Reveal Increased State Switching in the At-Risk Stage for Psychosis

Diana Wotruba^{1,2}, Thomas Bolton^{3,4}, Roman Buechler¹, Anastasia Theodoridou^{1,5}, Wulf Rössler^{1,6}, Dimitri Van de Ville^{3,4}, Karsten Heekeren¹

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A fundamental feature of the human brain is its intrinsic organization into anticorrelated functional networks. The right anterior insula (rAI) has been proposed to play a causal role in regulating the competing activity of the Default-Mode (DMN)- and Task-Positive Network (TPN). A disturbed network-coordination has been associated with the confusion of internally and externally focused attention. Thus, the aim of this study was to examine the dynamic fluctuations of spontaneous brain activity in order to test to what extent rAI co-activation patterns (CAP) would be disturbed in the at-risk state for psychosis. Using resting-state fMRI data we characterized the dynamic fluctuations of spontaneous brain activity by probing rAI interactions through CAP-analysis in 28 subjects with basic symptoms, 19 suffering from attenuated and/or brief limited intermittent psychotic symptoms, and 29 controls. In controls, the most frequent state displayed was rAI-TPN co-activation while the DMN was deactive, the second a rAI/DMN coactivation. Both at-risk groups engaged in shorter excursions in any state of rAI-coactivation and had a significantly smaller occurrence rate of the first state. The findings substantiate the pivotal role of rAI in governing TPN-to-DMN transitions, which seems to be dysfunctional in the psychosis at-risk state. Here, it is less likely to be active in concert with TPN-activation and DMN-deactivation and less able to remain active as part of a brain network, denoting increased state switching. This is, interestingly, regardless of symptom constellation.

Question and Answer Period

Discussant: Stephan Ruhrmann, Department of Psychiatry and Psychotherapy, University of Cologne, Cologne, Germany

affective and schizophrenic psychoses has been increasing, even during childhood. Potential risk factors have been indicated, such as familiarity, childhood adverse events, prenatal infection, cannabis abuse, with increasing risk of conversion when multiple risk factors are associated. Still, programs dedicated to identify pre-psychoses lack in Italy and the pathophysiology is not completely elucidated. Moreover, despite significant advances of biological psychiatry, there has been little progress in resolving the complex clinical phenotype of psychosis. In this context, the search for common and unique endophenotypes for major psychoses is an innovative and very compelling issue based on the increased degree of overlap in the pathophysiology of schizophrenia (SCZ) and bipolar disorder (BD). This has renewed interest in the validity of the Kraepelinian dichotomy. In addition, there is evidence that the exposure to specific environmental factors such as psychosocial and prenatal stress could result in different patterns of behavioural problems in adolescence. In this symposium we will present three major Italian research programs on adolescents and psychopathology trying particularly to deepen the potential additive factors in the ultimate expression of psychosis and emotional-behavioural problems. Also, as per an international perspective, a consistent early intervention program will be presented at the end of the symposium.

Talk 1

Research Programs on Juvenile Populations with Developmental Psychopathology Funded by the Italian Ministry of Health

Paolo Brambilla

University of Milan, Milan, Italy

In our research programs (SPES, WM?P) funded by the Italian Ministry of Health have mainly focused on children and adolescents with emotional and behavioural problems and have investigated personality and psychotic traits in twin populations. An integrated and multidisciplinary approach has been implemented including psychopathological, neuropsychological, neuroimaging, neuroimmunological, and genetic evaluations. Our programs are in line with the initiative of the NIH Research Domain Criteria (RDoC), trying to overcome diagnoses as only supported by symptom description. Several centres across North of Italy has participated in our research programs, including centres of the IRCCS "E. Medea" (Dr. Nobile, Prof. Fabbro, Dr. Molteni), the IRCCS San Raffaele of Milan (Dr. Furlan), the Programma2000 of Niguarda Hospital in Milan (Dr. Meneghelli, Dr. Monzani), and national twin surveys have been conducted in collaboration with the National Twin Registry of the Italian Institute of Health in Rome (Dr. Stazi, Dr. Fagnani). We will show the preliminary findings of such multimodal multi source dataset.

Symposium Session 24

Friday, October 21, 4:30–6:00 p.m., Manzoni

Major Italian Programs on Early Identification and Characterisation of Children and Adolescents at Risk for Psychopathology

Chair: Ernesto Caffo¹, Co-Chair: Frauke Schultze-Lutter²

Speakers: Paolo Brambilla, Alberto Parabiaghi, Paolo Fiori Nastro, Benedicto Crespo-Facorro

¹Università di Modena e Reggio Emilia, Modena, Italy, ²University of Bern, Germany

Major psychoses, such as schizophrenia (SCZ) and bipolar disorder (BD) are very common and severe diseases. The onset is usually during adolescence, with devastating effects on school and functioning, representing a high cost for the community. The prevalence of

Talk 2

Integrated Actions to Improve the Early Identification and Treatment of Vulnerable Youth Groups at Risk For Serious Mental Disorders

Alberto Parabiaghi¹, Barbara D'Avanzo¹, Mauro Percudani²

¹IRCCS Istituto di Ricerche Farmacologiche 'Mario Negri', Milan, Italy,

²Director Department of Mental Health at AOG Salvini, Garbagnate Milanese, Milan, Italy

Background: In the 2000s, a number of early psychosis teams were created in Italy to promptly ensure patients' engagement with best-possible psychosocial treatments. The present study explores the feasibility of the translation of the ultra-high risk (UHR) model into Italian community mental health services in order to move their action towards a more prevention-oriented approach.

Methods: This study, funded by the National Centre for Disease Prevention and Control, aimed at assessing the feasibility of the proposed prevention model, by uncovering the barriers within Italian mental health system and by evaluating the prospects for success in terms of clinical activity, recruitment flow, and patients' characteristics.

Results: During the past two years a model of service organization was developed and applied to six Italian mental health departments. Coordinated actions to improve the integration between child and adult mental health services, the accessibility to services for young and adolescents, the competence on the assessment and treatment of UHR individuals, and the capacity to deal with vulnerable groups like first- and second-generation immigrants were performed. Local community coalitions for improving awareness on the need for mental health prevention, and for ameliorating community's ability to deal with this problem were established. As by December 2015, a total of 215 subjects, aged 15-24 years, were assessed by the study teams with a prevalence of UHR individuals ranging 2-21%.

Conclusions: The UHR model with integrated community coalition proved transferability to Italian services. Some pitfalls and barriers were identified and discussed. There is concern about its long-term sustainability.

Talk 3

PhD Course on "Early Detection And Prevention Of Severe Mental Illnesses." An Italian Perspective

Paolo Fiori Nastro, Massimo Biondi, Paolo Girardi

Sapienza University of Rome, Rome, Italy

Worldwide mental disorders represent a striking and growing challenge for health systems in developed and developing regions. The peak of onset of mental disease is from the early teens to the mid-twenties. The early intervention paradigm advocates detecting and treating mental illness at their earliest stages, with the goal of influencing the trajectory of illness evolution. This is not a simple task. In most countries, including Italy, child and adolescents mental health services are separated from adult services; this lack in continuity of care has been described as the "weakest link in a system where it should be most robust". To promote a cultural change allowing a valid and different clinical approach to mental health, from 2008 Sapienza University of Rome has established a PhD course on "Early detection of mental illness". Since then, in collaboration with other foreign institutions, researches mainly focused on diagnostic aspects of UHR states, combining more diagnostic criteria centred on psychopathological aspects (i.e. basic symptoms and self disorders), as well as on psychotherapeutic interventions. Promotion of these research issues needs to be strongly supported in the future.

Talk 4

What We Talk About When We Talk About Specialized Early Intervention Programs: 15 Years of PAFIP (Cantabria, Spain)

Benedicto Crespo-Facorro

University of Cantabria, Santander, Spain

Specialized early intervention program in Cantabria (Programa Asistencial Fases Iniciales de Psicosis, PAFIP) was initiated in 2001 with the aims of shortening time of undetected non-affective psychosis, to provide acute care during first break of the illness, and to set up a recovery-oriented service offered over at least a 3-year period following first contact with PAFIP. During the former 15 years more than 590 individuals, and their cares, have been initially treated and followed in PAFIP. PAFIP is a team-based that rely on a multi-element approach to facing the illness with a personalized evaluation of needs and with several interventions (case management, group or individual psychotherapy, supported employment, educational programs, family intervention and education, suicide risk detection and intervention, treatment optimization (lower effective doses, monotherapy, AEs detection) with a focus on recovering individuals with a first episode of psychosis. Only if special treatment requirements are need, clients remain in PAFIP beyond 3 years and eventually they transit to regular services at community mental health services. , social workers, nurses and work counsellors—i.e., p and Psychiatrists, nurses and social worker and psychologists are primarily responsible for case management, pharmacotherapy, individual and family therapy, and coordination with primary healthcare. Allied health professionals generally provide supportive employment and rehabilitation and education services. Weekly team meetings and frequent communication among passionate team members bolsters commitment to the early intervention model, focuses treatment on each client's recovery goals and needs, and builds interdisciplinary team spirit that sustains high-quality service provision over time.

Question and Answer Period

Discussant: Maria Nobile, *Child Psychopathology Unit, Scientific Institute, IRCCS Eugenio Medea, Bosisio Parini, Lecco, Italy*

Symposium Session 25

Friday, October 21, 4:30–6:00 p.m., Foscolo

Mechanisms and Outcomes of Novel Psychological Interventions Targeting Social Recovery in Young People with At Risk Mental States and Psychosis

Chair: Kathryn Greenwood¹, Co-Chair: David Fowler²

Speakers: Clio Berry, Brioney Gee, Paul French, Kathryn Greenwood

¹University of Sussex, ²Sussex Partnership NHS Foundation Trust, UK,

²University of Sussex, UK

This symposium will present data from 4 novel mixed-methods studies, that aim to understand how hope, relationships, stigma and negative symptoms influence social and functional outcomes in the at risk mental state and psychosis. Data from both large quantitative data sets, and focussed qualitative studies are included. The second half of the symposium will present the outcomes of two novel psychological interventions to promote enhanced engagement and functional outcomes in these populations. PRODIGY is a definitive Randomised Controlled Trial of Social Recovery focussed Cognitive Behaviour Therapy in young people with Emerging Mental Health problems. This report on the internal pilot study will describe client characteristics and outcomes for the first 100 participants. Finally, the Early Youth Engagement in first episode psychosis (EYE) project will present the development and piloting of a new service level youth early youth engagement model on disengagement outcomes, as well as a range of other outcomes including communication, social involvement, relationships, hope and trust. Collectively these studies are at the forefront of new approaches to the development of psychological interventions in psychosis which have moved away from a primary focus on symptom reduction to recovery oriented outcomes. This focus is in tune with patient preferences, and provides data which is readily understandable in terms of policy makers and health economic demands. The studies offer considerable promise to intervene and address social disability and negative symptoms which are outcomes long neglected but are at the core of longer term social impacts of psychotic illness.

Talk 1

Hopefulness as a Mechanism for Promoting Positive Social Outcomes in Early Psychosis

Clio Berry¹, Victoria Bonnett², Sue Holtum², Sara Meddings
Ross Robinson¹, David Fowler¹, Kathryn Greenwood^{1,3}

¹University of Sussex, UK, ²Salomons Clinical Training Course, Canterbury Christchurch University, UK, ³Sussex Partnership NHS Foundation Trust, UK

Background: Hope, 'the will and the way' to achieve goals, is often mentioned as a 'non-specific' factor in psychological treatment outcome and perhaps especially important to recovery in psychosis. Yet empirical investigations of how and how much hope impacts on outcome in psychosis are limited. This paper will present hope as a key mechanism by which community psychiatric care facilitates positive social outcomes in psychosis.

Methods: A quasi-longitudinal study in early psychosis (N = 51, 18–36 years) used directed path analysis with measures of self-stigma, therapeutic relationship and professional expectations of a key community professional obtained at time 1 and hopefulness and social inclusion at time 2. Findings will also be presented from narrative analysis of hope stories in early psychosis (N = 10, 16–26 years) and larger studies in non-clinical populations.

Results: A large association between hopefulness and social inclusion was observed in the quasi-longitudinal study in psychosis. Path analysis supported hopefulness as a mediator of the association between

pre-existing self-stigma and outcome. Additionally, data support hopefulness as a mechanism by which community psychiatric care facilitates social inclusion; through community professionals inspiring hope within positive therapeutic relationships and optimistic expectations. Complimentary findings from narratives of hope in early psychosis will be shared. Larger studies of hopefulness and social outcomes in non-clinical populations will indicate a particularly important role for hopefulness in youth mental health.

Conclusions: Hopefulness represents a potentially key mechanism to facilitate positive social outcomes in early psychosis and mitigate the impact of negative self-beliefs and experiences; especially for adolescents.

Talk 2

The Relationship Between Social Recovery and Negative Symptom Course in First-Episode Psychosis: Insights from a Mixed-Methods Approach

Brioney Gee¹, Jo Hodgekins¹, David Fowler², Caitlin Norey¹

¹University of East Anglia, Norwich, UK, ²University of Sussex, UK

Purpose: Negative symptom severity has been identified as a significant predictor of poor recovery following first-episode psychosis. This study aimed to: (a) investigate the relationship between early negative symptom course and concurrent social recovery, and (b) explore the understanding and experience of recovery of individuals with differing early negative symptom trajectories.

Materials and Methods: The early negative symptom and social recovery trajectories of 764 Early Intervention in Psychosis service-users (participants in the EDEN study) were examined. Negative symptoms trajectories were established using latent class growth analysis to model PANSS data, social recovery trajectories by using the same technique to model structured time-use measured using the Time Use Survey. The association between negative symptom and social recovery trajectory class membership was examined statistically. Next, transcripts of in-depth interviews with a purposive subsample of participants were analysed thematically in order to explore lived-experiences of recovery.

Results: Negative symptom and social recovery trajectories were not independent of one another ($\chi^2 = 57.06$, $p = <0.001$). Where elevated negative symptoms are present at baseline, whether or not they remit, they are associated with poor social recovery. Those with differing early negative symptom trajectories had contrasting understandings and experiences of recovery.

Conclusions: Early negative symptom severity is associated with poor social recovery, even when these symptoms remit. Differences between the accounts of recovery given by those with differing early negative symptoms courses may provide clues as to the nature of the relationship between negative symptom severity and poor social recovery following first-episode psychosis.

Talk 3

PRODIGY: Prevention of Long Term Social Disability Amongst Young People with Emerging Mental Health Problems: A Definitive RCT of Social Recovery Focused CBT

Paul French¹, Tim Clarke², David Fowler³

¹University of Manchester, UK, ²University of East Anglia, UK,

³University of Sussex, UK

Background: Outcome studies of young people with At Risk Mental states have consistently identified that those at greatest risk are young people who present with social decline, alongside sub-threshold psychosis. The focus of intervention in this group has been on prevention of psychosis symptoms. This trial aimed to identify and target the group of young people who are socially disabled, with severe At Risk mental health problems and to evaluate the efficacy of a new psychological intervention specifically tailored to their needs.

Methods: The study is the first large, definitive, blinded, randomised controlled treatment trial in this area, comprising a 9-month intervention and 15-month follow up of 135 treatment cases and 135 controls in three centres. The intervention involves a multisystemic CBT approach, promoting a sense of agency, hope, motivation and activity whilst managing psychotic and other symptoms and problems, compared to Enhanced Standard Care (ESC). The primary outcome is hours per week engaged in constructive activity.

Results: Client characteristics and outcomes are reported from the first 100 participants in the internal pilot, as well as qualitative data on participants' experiences of therapy. Participants had extremely low activity levels, typically fewer than 9 hours per week, extreme social withdrawal, paranoia, social anxiety, depression and emerging negative symptoms.

Conclusions: Intervention in this population is of major importance as this group is at the highest risk of the poorest long-term outcomes. These are a challenging group to engage and treat but the strategies adopted indicate the potential and promise for effective intervention.

Talk 4

The Early Youth Engagement (EYE) Project: A Feasibility and Pilot Study to Promote Better Engagement and Outcomes in First Episode Psychosis

Kathryn Greenwood^{1,2}, Kirsty Labuschagne¹, Ruth Chandler¹, Emmanuelle Peters³, Katie Alford¹, Richard deVisser², Andy Field², Philippa Garety³

¹Sussex Partnership NHS Foundation Trust, UK, ²University of Sussex, UK, ³Institute of Psychology, Psychiatry and Neuroscience, Kings College London, England

Background: Engagement with Early Intervention in Psychosis (EIP) services improves symptoms, illness course, social and occupational function, yet, 25-30% of patients disengage from services within the first 12 months. This study aimed to develop an intervention to promote better youth engagement and health outcomes for this population.

Method: First, a cross-sectional qualitative study investigated facilitators and barriers to engagement from the perspective of EIP service users, their relatives and healthy young people. Forty focus groups/interviews were conducted with 68 participants, and thematic analysis was applied to the transcribed data. Next, a Delphi consultation with 27 clinicians, managers and experts, reached consensus on a set of pragmatic, deliverable service adaptations which formed the new Early Youth Engagement (EYE) service model. Finally, 298 first episode psychosis services users received either the original model (pre-adaptation) or the EYE model (post-adaptation), and both engagement at 12 months, and feasibility and satisfaction were explored.

Results: A generalized linear model with engagement status nested within teams, revealed that the proportion disengaged was

significantly lower in the EYE model cohort. Engagement was not predicted by team, age or gender. Disengagement decreased from 24% prior to 14.5% post the intervention. Qualitative feedback revealed impacts on communication, social involvement, staff approaches, collaboration, practical goals, hope and trust.

Conclusion: This study demonstrates how a new early youth engagement model might reduce drop out, and promote satisfaction and better social and health outcomes for this sub-group of young people at risk of disengagement.

Symposium Session 26 Saturday, October 22, 1:00–2:30 p.m., Washington A

Early Intervention Services for First-Episode Psychosis: How long?

Chair: Ashok Malla¹, Co-Chair: Merete Nordentoft²

Speakers: Eric Chen, Nikolai Albert, Srividya Iyer, Ashok Malla

¹McGill University, Montréal, Canada, ²University of Copenhagen, Mental Health Centre Copenhagen, Denmark

Specialized Early Intervention (SEI) services for first-episode psychosis are shown to have positive effects on positive and negative symptoms, medication adherence, relapse, substance abuse, functional outcome and quality of life after two years of treatment. However, follow up studies suggest that these benefits are not maintained when SEI is not sustained beyond 2 years. A Canadian study (Norman et al 2011) showed that, by maintaining patients in an EI service with even a lower intensity of service, benefits accrued after 2 years of SEI service were largely maintained at 5 years unlike the OPUS study where the benefits were lost when patients were transferred to regular care after 2 years of SEI. The objective of this symposium is to present the results of three different clinical trials conducted in three different countries with different service systems to answer the question whether extending SEI services beyond the first 2 years provides greater benefits than are achieved in regular care. Chen will present results of two studies conducted in a low-resource environment in Hong Kong. This will be followed by results of two randomized controlled trials conducted in Copenhagen (Denmark) and Montréal (Canada), to be presented, respectively, by Albert and Iyer. The fourth presentation by Malla will synthesize insights from the findings of studies that explore the optimal duration of SEI. It will also highlight methodological learnings and propose future directions. Finally, Birchwood will discuss the results of these studies in the context of the concept of the 'critical period' hypothesis.

Talk 1

Critical Period in Early Psychosis Intervention: Possible Dose Effect From Longitudinal Studies from Hong Kong

Eric Chen, Wing Chung Chang, Edwin Lee, Kit Wa Sherry Chan, Christy Hui

University of Hong Kong, Hong Kong

Purpose: The critical period hypothesis – that the outcome of psychosis is largely determined within the first few years – constitutes a rationale for focusing psychosis intervention resources on the early years. This hypothesis predicts that intervention in the initial years yields better outcomes that are maintained in the subsequent post-intervention years. Since 2001, Hong Kong has provided two years of specialised early service to patients with first-episode psychosis aged 15 to 25. Controlled studies suggest that this yielded improved outcomes that were sustained for up to 10 years. This suggests an overall efficacy of intervention consistent with the critical period hypothesis. We further explored enhancing the intervention with an additional year of service.

Method: Patients completing two years of intervention were randomised to receive either one more year of intervention (three years total), or to transition to a year of standard care.

Results: The functioning of patients receiving an additional year of intervention continued to improve in the third year, while that of the control group remained unchanged. However, the effects of this additional year did not persist, largely due to catch-up in the group which did not receive additional intervention.

Conclusion: We conclude that after two years, further outcome improvements could be effected. Our observations are suggestive of a dose effect of intervention. The critical period effect is evident with lower-level input, but with more input, the additional benefit did not persist. The validity of the critical period hypothesis is not uniform and appears contingent upon the intensity of intervention.

Talk 2

How Long Should Early Intervention Last? Results from a Randomized Clinical Trial of the Effect of Five-Years versus Two Years Specialized Assertive Intervention for First Episode Psychosis – The OPUS-II Trial

Nikolai Albert^{1,2}, Carsten Hjorthøj^{1,2}, Heidi Jensen¹, Marianne Melau¹, Ole Mors³, Charlotte Emborg³, Merete Nordentoft^{1,2}

¹Mental Health Centre Copenhagen, Denmark, ²University of Copenhagen, Denmark, ³Center for Psychiatric Research, Aarhus University Hospital, Denmark

Purpose: The OPUS I trial found that it was possible to improve clinical outcome in first episode psychosis through a specialized early intervention service (SEI). However, the five-year follow-up showed that few of the positive clinical effects were sustained when the intensive treatment was terminated. The question arose whether two years of SEI were too short. This represents the rationale for the OPUS II-trial, investigating if five years of SEI treatment is more appropriate to ensure long lasting clinical effect.

Materials and Methods: The OPUS II trial recruited 400 patients from the now established OPUS teams. Patients were randomized to three further years of OPUS treatment or transfer to standard treatment. The primary outcome is negative symptoms. Secondary outcomes are, psychotic- and disorganized symptoms, client satisfaction, hospitalization, labour marked affiliation, substance abuse, working alliance, medication and self-efficacy.

Results: The study did not find any effect on the primary outcome or any of the functional or psychopathological outcomes. We did find that patients in the prolonged OPUS group had a stronger working alliance with their case manager and were more content with their treatment.

Conclusion: Based on the results we don't believe that the OPUS treatment in its current form should be extended, but we will discuss the implications of delayed treatment start and developments within the standard treatment which might shed light on the lack of results. Also sub-group analyses are needed to establish if some groups benefit more from the prolonged treatment.

Talk 3

A Randomized Controlled Trial of Extended Specialized Early Intervention Verses Specialized Early Intervention Followed by Regular Care for Treatment of Early Psychosis over the Five Year Critical Period

Srividya Iyer^{1,2}, Ashok Malla^{1,2}, Ridha Joobar^{1,2}, Ross Norman³, Eric Latimer¹, Norbert Schmitz¹, Eric Jarvis¹, Howard Margolese¹, Amal Abdel-Baki⁴, Sherezad Abadi², Sally Mustafa², Danyael Lutgens¹

¹McGill University, Montréal, Canada, ²Prevention and Early Intervention Program for Psychosis (PEPP), Douglas Mental Health University Institute, Montréal, Canada, ³Western University, Ontario, Canada, ⁴University of Montréal, Montréal, Canada

Purpose: The objective of this trial was to test the effectiveness of a 3-year extension of specialized early Intervention (SEI) beyond the initial 2 years of SEI compared to 3 years of regular care following 2 years of SEI.

Methods: Patients were randomized following 2 years of SEI to receive either 3-years of continued EI or regular care. Blinded evaluations on multiple outcome variables were conducted every three months. Remission (proportion and length) of positive and negative symptoms was the primary outcome. 220 patients were randomized to either extended SEI (n = 109) or to regular care (n = 111).

Results: Preliminary survival analysis results show a significantly lower rate of and a longer time to disengagement from treatment for the SEI group compared to "regular care" (22% vs 58%, respectively, $p < .001$; 32 vs 23 months, $p < .001$). Patients receiving extended SEI were in positive symptom remission for a longer period than those in regular care (23 vs 17 months, $p < .001$); the difference in length of total remission was not significant; and there were no differences in relapse rates. Full analyses for all primary and secondary outcomes, including service utilization and economic consequences, will be conducted in the summer of 2016.

Conclusion: Our preliminary findings suggest that providing EI throughout the critical period of 5 years may facilitate better outcomes than SEI followed by regular care. Findings from this study have implications for service provision in first-episode psychosis. Challenges of a service-based study and attrition from research evaluations will be discussed.

Talk 4

The Optimal Duration of Specialized Early Intervention Services for Psychosis: The State of the Field and Future Directions

Ashok Malla¹, Merete Nordentoft², Srividya Iyer¹

¹McGill University, Montréal, Canada, ²University of Copenhagen, Denmark

Purpose: The development of specialized early intervention (SEI) services for psychotic disorders has been one of the major achievements in mental health in the past 20 years. Although, substantial evidence for the effectiveness of SEI has been accumulating over the past decade, several challenges remain. Chief among them is the question of how long patients with first-episode psychosis require such specialized, resource-intensive services.

Method: A number of recent studies have addressed this question. This presentation will provide an overview of these studies, focusing on insights from their findings and key considerations about methodology, outcome variables and design for future studies.

Results: SEI yields better outcomes than regular care two years after treatment. However, Denmark's OPUS study found that most gains from two years' SEI were not sustained at five years. A Canadian study of regular SEI followed by three years of lower-intensity SEI reported sustenance of symptomatic benefits and further functional improvements in the last three years. Our team, the OPUS team and Chen's group in Hong Kong are concluding RCTs comparing extended SEI with SEI followed by regular care. Preliminary findings support an extension of SEI, but not unequivocally.

Conclusion: Findings of existing studies will be examined with respect to the "critical period" hypothesis. Discussion will also highlight methodological learnings and suggest future directions, such as targeted interventions for those less likely to functionally improve, custom durations (longer EI for more vulnerable patients), and differing delivery modes (complete or stepped-down; complete or regular care supplemented by tele-SEI, etc.).

Question and Answer Period

Discussant: Max Birchwood, Mental Health and Wellbeing, Warwick Medical School, Coventry, UK

On this basis we will then explore some recent data on possible mechanisms which may underlie this link and investigate how collaboration with basic neurosciences in the framework of translational research may bring us a step further in our understanding of this issue and closer to potential specific treatments.

Talk 1

Childhood Trauma and the Onset and Outcome of Psychosis: What is the Evidence?

Helen L Fisher¹, Paola Dazzan¹, Julia Lappin¹, Margaret Heslin¹, Gillian Doody², Peter B. Jones³, Robin M Murray¹, Craig Morgan¹

¹King's College London, UK, ²University of Nottingham, Nottingham, UK, ³University of Cambridge, Cambridge, UK

Purpose: Increasing evidence suggests that exposure to traumatic events in childhood is linked to the emergence of psychotic disorders in adulthood. However, the impact of childhood trauma on the longer-term outcomes of psychosis is largely unknown. Therefore, this presentation will provide an overview of existing literature including a recent meta-analysis and provide novel data on the impact of childhood abuse on the course and outcomes of psychotic disorders over 10 years.

Methods: Data on 214 patients presenting for the first time to mental health services with psychosis was drawn from the UK Aetiology and Ethnicity of Schizophrenia and Other Psychoses (AESOP) study. Childhood abuse was assessed retrospectively using the Childhood Experience of Care and Abuse Questionnaire at baseline and extensive information on psychosis course and functional outcomes over 10 years was obtained via interviews and case-notes.

Results: Psychosis cases who reported exposure to physical, sexual or emotional abuse prior to age 17 were more likely to achieve remission within 6 months of first presentation than non-exposed cases (OR = 2.91). However, they were at increased risk of self-harm (OR = 3.3) and suicide attempts (OR = 2.3), had more severe positive psychotic symptoms (OR = 3.2) and were less likely to be employed (OR = 0.4) during 10-year follow-up.

Conclusion: Childhood trauma is associated with the onset of psychosis but its impact on clinical course of psychotic disorder remains unclear. However, initial findings suggest that Early Intervention Services should screen new patients for childhood abuse and be mindful that those exposed may require additional support to improve their functional outcomes.

Symposium Session 27

Saturday, October 22,

1:00–2:30 p.m., Washington B

Understanding the Trauma-Psychosis Link: Can Translational Research Bring Us a Step Further?

Chair: Philippe Conus¹

Speakers: Helen L Fisher, Luis Alameda, Daniella Dwir, Monica Aas

¹DP-CHUV, Lausanne University, Lausanne, Switzerland

Recent literature has repeatedly shown that trauma is more prevalent in psychosis patients than in control populations and thus trauma has been identified as a potential risk factor for the emergence of psychosis. In addition, several papers have shown that clinical outcome, both symptomatic and functional, is poorer in psychosis patients who have been exposed to trauma than in patients who haven't. Many hypotheses have been proposed to explain these correlations, but the possible underlying mechanisms remain largely unknown. In this symposium we will provide an overview of the association between exposure to childhood trauma and both the onset of psychosis and outcome of patients regarding symptoms and functional levels. We will also discuss how the age at the time of exposure to trauma may influence the correlation with symptomatic and functional outcome.

Talk 2

Age at the Time of Exposure to Trauma Modulates the Psychopathological Profile and the Impact on Functional Outcome in Early Psychosis Patients

Luis Alameda^{1,2}, Philippe Golay², Philippe S Baumann^{1,2}, Carina Ferrari^{1,2}, Mhedi Gholam-Rezaee³, Kim Q Do², Philippe Conus¹

¹Center for Psychiatric Neuroscience, Department of Psychiatry, Lausanne University Hospital (CHUV), Switzerland, ²Service of General Psychiatry, Treatment and Early Intervention in Psychosis Program (TIPP-Lausanne), Lausanne University Hospital (CHUV), Switzerland, ³Department of Psychiatry, Center for Psychiatric Epidemiology and Psychopathology, Lausanne University Hospital (CHUV), Switzerland

Objectives: We aim to examine, in a sample of Early Psychosis (EP) patients treated in a specialized program during three years, the potential differential impact of childhood trauma, according to age at the time of exposure, on the level of functioning and on the psychopathological profile of patients during the early phase of the disease.

Methods: 225 EP subjects aged 18-35 were followed-up prospectively over 36 months. Patients who had faced at least one experience of abuse or neglect were classified according to age at the time of first exposure (Early-Trauma: before age 12; Late-Trauma: between age 12 and 16), and then compared with unexposed patients (Non-Trauma). The level of symptoms was assessed using the Positive and Negative Syndrome Scale, The Young Mania Rating Scale, and the Montgomery-Asberg Depression Rating Scale. The level of functioning was assessed with the Global Assessment of Functioning.

Results: Comparisons over the 3 years of treatment with the Non-Trauma patients revealed that (i) Early-Trauma patients showed consistently higher levels of positive ($p = 0.006$) depressive ($p = 0.001$), manic ($p = 0.006$) and negative ($p = 0.029$) symptoms and had poorer functional level ($p = 0.025$) (ii) Late-Trauma patients only showed more negative symptoms ($p = 0.029$).

Conclusions: The age at the time of exposure to trauma has a modulating effect on its impact on symptoms and functional impairment in EP patients. Various biological and psychological hypotheses can be proposed to explain this observation, and they need to be investigated in experimental setting in order to develop therapeutic avenues.

Talk 3

Early-Life Insults Impair Parvalbumin Interneurons via Oxidative Stress: Prevention and Reversal by N-Acetylcysteine and Environmental Enrichment

Daniella Dwir, Jan-Harry Cabungcal, Pascal Steullet, Michel Cuenod, Kim Q Do

Center for Psychiatric Neuroscience, Department of Psychiatry, University Hospital of Lausanne, Switzerland

Purpose: A hallmark of the pathophysiology of schizophrenia is a dysfunction of parvalbumin-expressing fast-spiking interneurons (PVI), which are essential for neuronal synchrony during sensory and cognitive processing. Oxidative stress as observed in schizophrenia affects PVI. Some schizophrenia patients have decreased brain glutathione (GSH) levels due to genetic and functional origin. GSH dysregulation, by increasing vulnerability to oxidative stress, could lead to cortical circuit anomalies during specific developmental windows.

Methods: We used mice with impaired synthesis of glutathione (Gclm knockout [KO]) to investigate the effect of redox dysregulation and additional insults at various periods of postnatal development on maturation and long-term integrity of PVI in the anterior cingulate cortex.

Results: A redox dysregulation, as in Gclm KO mice, renders PVI vulnerable to exhibit oxidative stress. A glutathione deficit delays PVI maturation and their perineuronal net. An additional oxidative

challenge in young, but not adult KO mice, reduces the number of PV-immunoreactive interneurons. The effect of early-life insults on PVI can be prevented with N-acetylcysteine (NAC) treatment from pregnancy until pubertal. Early-life insults have long-term consequences on PVI, which can also be reversed with combined NAC treatment and Environmental Enrichment during childhood and adolescent.

Discussion: In analogy, individuals carrying genetic risks to redox dysregulation potentially vulnerable to early-life insults could benefit from a combined pharmacological and psycho-social therapy. These data support the need to develop novel therapeutic approaches based on antioxidant and redox regulator compounds, which could be used in combination with cognitive behavioural therapy, as preventive treatment in young at-risk subjects.

Talk 4

Childhood Trauma is Associated with Increased Brain Responses to Emotionally Negative as Compared to Positive Faces in Patients with Psychotic Disorders

Monica Aas¹, Christine L Brandt¹, Karolina Kauppi¹, Martin Tesli¹, Tobias Kaufmann¹, Nils E Steen², Lars T Westlye^{1,3}, Ingrid Agartz^{1,4}, Ole A Andreassen¹, Ingrid Melle¹

¹NORMENT K.G. Jebsen Centre for Psychosis Research, Institute of Clinical Medicine, University of Oslo, and Division of Mental Health and Addiction, Oslo University Hospital, Oslo, Norway, ²Drammen Outpatient Clinic, Clinic of Mental Health and Addiction, Vestre Viken Hospital Trust, Drammen, Norway, ³Department of Psychology, University of Oslo, Norway, ⁴Department of Psychiatric Research, Diakonhjemmet Hospital, Oslo, Norway

Background: Childhood trauma increases risk of developing psychosis. However the mechanisms are elusive. Here, we tested the association between childhood trauma and brain activation during a face processing task in patients diagnosed with psychosis continuum disorders. We also tested if the high trauma group rated negative faces as more negative and positive faces as less positive than the group with no or low trauma.

Methods: We included 101 patients with a DSM-schizophrenia spectrum or bipolar spectrum diagnosis. History of childhood trauma was obtained using the Childhood Trauma Questionnaire (CTQ). Brain activation was measured with functional MRI during processing of faces with negative or positive emotional expressions. After the scanner session, patients rated how negative or positive they experienced the faces on a rating scale.

Results: Compared to patients with no or low levels of childhood trauma, patients with high levels had higher BOLD signal for negative than positive faces in the inferior frontal gyrus, right middle frontal gyrus, right cerebellum, the inferior/superior parietal and occipital lobe, with moderate to large effect sizes (Cohen's $d = 0.70-0.93$). The largest effect was observed for the parietal lobe and the supra-marginal gyrus. In patients with schizophrenia, childhood trauma was also associated with reporting negative faces as more negative, and positive faces as less positive (Cohen's $d > 0.8$).

Conclusions: Along with the observed negativity bias in the assessment of emotional valence of faces, our data suggest increased brain responses to negative faces and reduced responses to positive faces in patients with childhood trauma.

Symposium Session 28

Saturday, October 22, 1:00–2:30 p.m., Manzoni

The PRONIA Study: An Integrated European Multidisciplinary Approach to Prevent Psychosis at Individual Level

Chair: Nikolaos Koutsouleris¹, Co-Chair: Paolo Brambilla²

Speakers: Stephan Ruhrmann, J Kambeitz, H Pesonen, E Meisenzhal

¹University of Munich, Munich, Germany, ²University of Milan, Milan, Italy

The PRONIA (grant agreement n. 602152) is an EU-funded project aiming at classifying the risk to develop psychosis and depression by integrating multimodal (clinical, imaging, cognitive, genetic) data and by using machine learning techniques. Six European centres are currently participating (Munich, Cologne, Basel, Milan, Turku, Birmingham) and about 900 subjects have been recruited so far. In this symposium we will present the general framework of the study with particular regards to clinical, imaging and genetic data in the context of personalised medicine. First, the relationship between functional domains and clinical variables will be elucidate in high risk and psychotic patients. Then, new imaging findings using the BrainAGE approach will be presented including genetic and environmental factors. Successively, machine learning classification of modelling clinical heterogeneity of psychosis and depression will be debated. Finally, strategies of early recognition services through broadly available telemedical applications will be presented in the framework of PRONIA's dataset. PRONIA consortium is indeed developing an eHealth prototype providing telepsychiatric services for an accurate prediction of mental health related disabilities in young help-seeking persons; diagnostic tools and medical device technologies in personalised medicine will be presented. This symposium will therefore provide preliminary and fascinating results on an ongoing European multicenter study which will be of great help in the next few years to disentangle the pathophysiology of psychosis and depression, ultimately helping in planning innovative and personalised approaches to prevent and early recognise psychosis and depression.

Talk 1

Functional Deterioration and Its Clinical Predictors in Subjects Clinically at High Risk of Psychosis and Patients with a Recent Onset Psychosis

Stephan Ruhrmann¹, M Rosen¹, N Kaiser¹, T Haidl¹, F Schultze-Lutter¹, S Borgwardt², P Brambilla³, C Pantelis⁴, R Salokangas⁵, E Meisenzhal⁶, S Wood⁷, N Koutsouleris⁶

¹University of Cologne, Köln, Germany, ²University of Basel, Switzerland,

³University of Milan, Italy, ⁴University of Melbourne, Australia,

⁵University of Turku, Finland, ⁶University of Munich, Germany,

⁷University of Birmingham, UK

Background: Functional deterioration has become an important topic in research on clinical high risk states as social and role performance proofed to be markedly impaired already in this early, putatively prodromal condition. Furthermore, despite remission of symptomatic risk indicators, functional decline persists in a considerable amount of CHR subjects. A better understanding of composition and determinants of functional impairment is therefore essential, particularly, as current interventions can prevent a transition to psychosis, but do not equally well improve social and role performance.

Method: PRONIA ('Personalized Prognostic Tools for Early Psychosis Management') is a prospective collaboration project funded by the European Union under the 7th Framework Programme (grant agreement n° 602152). Seven university centres in five European countries

and in Australia participate in the evaluation of three clinical groups (subjects clinically at high risk of developing a psychosis [CHR], patients with a recent onset psychosis [ROP] and patients with a recent onset depression [ROD]) as well as healthy controls. Functioning is not only measured by global scales of functioning, but also by the Functional Remission in General Schizophrenia Scale (FROGS), comprising five domains.

Results: In all patient groups, functioning was impaired. In a preliminary interim analysis, the FROGS, but none of the more global measures differentiated between CHR and ROD in two domains, where the CHR had a position in-between ROP and ROD. Discussion: We will further elucidate these results and present an analysis of the relationship between functional domains and clinical variables in CHR and ROP.

Talk 2

BrainAGE Approach: Investigating Ageing-related Patterns of Brain Maturation in the Context of Psychosis

J Kambeitz¹, C Cabral¹, L Kambeitz-Illankovic¹, M Re², S Borgwardt³, S Ruhrmann⁴, R Salokangas⁵, S Wood⁶, E Meisenzhal¹, P Brambilla², N Koutsouleris¹

¹University of Munich, Germany, ²University of Milan, Italy, ³University of Basel, Switzerland, ⁴University of Cologne, Köln, Germany, ⁵University of Turku, Finland, ⁶University of Birmingham, UK

There is evidence from multiple lines of research indicating alterations in brain structure and function in patients with psychiatric disorders such as schizophrenia or major depressive disorder. The pathophysiological mechanisms underlying these changes remain largely unknown until today. The current debate is focused on the time of onset of brain alterations (perinatal vs. prodromal vs. illness-onset) and their trajectory (progressive vs. non-progressive). The BrainAGE approach (Brain 'Age Gap Estimation') represents a statistical modelling framework that allows the conceptualisation of functional or structural brain alterations in individuals as deviations from a normative trajectory of maturational/ageing-related patterns. Using multivariate statistical methods, BrainAGE has successfully been applied to different psychiatric populations. New findings from the PRONIA study using the BrainAGE approach will be presented including the extension of the approach to further neuroimaging-modalities as well as the validation using genetic and environmental factors.

Talk 3

Improving Machine-learning Based Predictive Psychiatry via Subgroup-Sensitised Classification Methods: Results of the PRONIA Project

H Pesonen¹, R Salokangas¹, S Borgwardt², S Ruhrmann³, P Brambilla⁴, S Wood⁵, C Pantelis⁶, E Meisenzahl⁷, N Koutsouleris⁷

¹University of Turku, Finland, ²University of Basel, Switzerland,

³University of Cologne, Köln, Germany, ⁴University of Milan, Italy,

⁵University of Birmingham, UK, ⁶University of Melbourne, Australia,

⁷University of Munich, Germany

Purpose: In recent years, machine learning has arisen as one of the most interesting new approaches for early identification of at-risk mental states of psychosis. However, the biological heterogeneity within all clinical groups such as clinical high-risk subjects, healthy controls, subjects with recent onset of psychosis make it difficult to achieve great classification accuracy if this multi-modal heterogeneity within the populations is not explicitly modelled. Material and **Methods:** In the Personalised Prognostic Tools for Early Psychosis Management study (PRONIA) we explore techniques that decompose the heterogeneous population into homogeneous subgroups and use the attained clustering information to sensitise the classifiers to achieve better performance when separating subjects with recent onset of psychosis, clinical high risk subjects and healthy control populations from each other based various clinical and neurobiological data-modalities.

Results: Using premorbid, baseline clinical and neuroimaging (structural and functional MRI) data, we were able to separate patients with recent onset psychosis and clinical high-risk to psychosis from healthy controls reasonably well.

Conclusions: The suggested method of modelling heterogeneity of clinical disorders and using this information with machine learning classification seem to be promising approach to enhance classification of heterogeneous clinical disorders.

Talk 4

Diagnostic Tools and Medical Device Technologies in Personalised Medicine: Big Data Market Analysis of Medical Neuroscience

E Meisenzahl¹, P Brambilla², N Koutsouleris¹, C Pantelis³, S Ruhrmann⁴, R Salokangas⁵, S Wood⁶, S Borgwardt⁷, A Stellbrink¹

¹University of Munich, Germany, ²University of Milan, Italy, ³University of Melbourne, Australia, ⁴University of Cologne, Germany, ⁵University of Turku, Finland, ⁶University of Birmingham, UK, ⁷University of Basel, Switzerland

The PRONIA consortium is developing an eHealth prototype providing telepsychiatric services for an accurate prediction of mental health related disabilities in young help-seeking persons. This eHealth prototype will become available within the next five years and will pave the way for accurate, personalized diagnostics for persons at risk that can be implemented all over the world. PRONIA's ultimate goal is to achieve/realise licensing, commercialisation and sustained engineering strategies of its early recognition services through broadly available telemedical applications. The digitalization of information and communication processes as well as general computing advances over the last 15 years triggered a highly dynamic industrial revolution leading to the development of robots and artificial intelligence among other advances. In contrast, international health sectors have fallen behind with the implementation of IT solutions. The prospect of further global population increase, and thus further increase in chronic diseases, leads to rising costs due to increasing worldwide healthcare expenditure. In the presentation, the field of eHealth and the development of chronic diseases are defined. It provides an overview of the current state of eHealth diagnostic tools and eHealth applications in medical neuroscience. Using the strategy of big data analytics, opportunities and prospects of the eHealth market in

diagnostics and mobile health technology are evaluated, and will be discussed together with global medical technology landscape.

Question and Answer Period

Discussant: Stefan Borgwardt, University of Basel, Switzerland

Symposium Session 29 Saturday, October 22, 1:00–2:30 p.m., Foscolo

Schizotypy in Youths: Stress, Cognition and Relationships with Transition to Psychosis

Chair: Martin Debbané¹, Co-Chair: Frauke Schultze-Lutter²

Speakers: Neus Barrantes-Vidal, Maude Schneider, Eduardo Fonseca-Pedrero, Rahel Flückiger

¹University of Geneva, Switzerland, ²University of Bern, Switzerland

The assessment of schizotypy during adolescence and young adulthood bears crucial information on developmental interactions antedating the onset of psychotic disorders. Examining schizotypy along with key risk factors can thus critically inform early intervention programs seeking to delay or avoid transition to psychosis. A number of studies currently examine the early interactions between stress and schizotypy in exacerbating the first signs of risk for psychosis. Importantly, genetic factors appear to play a key role linking stress to early signs of schizotypy. In this symposium, two presentations will address the genetic-stress diathesis in at-risk populations. First, Dr Barrantes-Vidal will present a dataset combining experience sampling to genetic analyses on stress sensitivity genes to understand the contributions of childhood adversity on psychosis expression, in both non-clinical subjects rating high on schizotypy and subjects diagnosed with at-risk mental states for psychosis. Next, Dr Schneider will present original research on the impact of stressful life events in exacerbating the expression of schizotypy in youth with 22q11.2 deletion syndrome, a condition associated with a 30% prevalence of psychotic disorders. Following these two presentations, Dr Fonseca Pedrero will focus on the relationship between cognition and schizotypy in determining the expression of significant schizotypal manifestations in community youths. Finally, Dr Flückiger will present how schizotypy can inform the question of conversion from clinical high risk states to psychosis, through the analysis of longitudinal data. Together, these presentations harbour the methods and results that are starting to uncover the key developmental interactions sustaining risk for psychosis.

Talk 1

Impact of Childhood Adversity, Genetic Variation, and their Interaction on Psychotic-like Symptoms and Stress Reactivity in Psychometric and Clinical High Risk Samples

Neus Barrantes-Vidal^{1,2,3,4}, Paula Cristóbal-Narváez¹, Tamara Tamara¹, Marta de Castro-Català⁵, Manel Monsonet¹, Lúdia Hinojosa¹, Anna Racioppi¹, Tecelli Domínguez-Martínez⁶, Elionora Peña⁵, Sergi Ballespí¹, Araceli Rosa^{4,5}, Thomas Kwapiil²

¹Universitat Autònoma de Barcelona, Barcelona, Spain, ²University of North Carolina at Greensboro, USA, ³Sant Pere Claver – Fundació Sanitària, Barcelona, Spain, ⁴Centre for Biomedical Research Network on Mental Health, ⁵Universitat de Barcelona, Barcelona, Spain, ⁶Cátedras-CONACYT/INPRF, Mexico

Purpose: This study examined whether childhood adversity, genetic variation, and their interaction play a role in stress reactivity and the expression of psychotic-like symptoms in daily life.

Materials and Methods: The Experience Sampling Method was used with 206 nonclinical young adults (oversampled for schizotypy) and 50 ARMS patients during one week to assess momentary negative affect, psychotic phenomena, and stress appraisals. Participants completed measures of childhood adversity and were genotyped for SNPs in relevant psychosis and stress-sensitivity genes (COMT, FKBP5 and OXTR).

Results: Both distal adversity and momentary situational and social stress appraisals were associated with the real-world expression of psychotic-like symptoms in both samples. In addition, childhood adversity was associated with increased stress reactivity. Overall, variability on COMT, FKBP5 and OXTR was scarcely associated with psychotic experiences and stress-reactivity. In nonclinical participants, the FKBP5 haplotype, number of COMT Met alleles and number of OXTR G alleles interacted with childhood adversity in the expression of stress reactivity. Analyses in the ARMS sample (so far completed for COMT) indicated that adversity increased psychotic-like symptoms only in Met carriers.

Conclusion: Findings concur with and extend prior research by supporting (i) the role of distal adversity in sensitizing individuals to momentary stress and how this impacts on psychotic reactivity in daily life, and (ii) the moderating effect of genetic variability across levels of psychosis risk. Investigating the interplay of adversity, genes, and current context seems relevant for uncovering mechanistic pathways to psychosis and should inform the development of ecologically valid intervention strategies.

Talk 2

Stressful Life Events Modulates the Expression of Positive Schizotypy in 22q11.2 Deletion Syndrome

Maude Schneider^{1,2}, Marco Armando^{1,2}, Martin Debbané^{1,2}, Stephan Eliez^{1,2}

¹University of Geneva, Geneva, Switzerland, ²Office Médico-Pédagogique, Geneva, Switzerland

Objective: 22q11.2 deletion syndrome (22q11DS) is recognized as a model for schizophrenia. In patients with 22q11DS, attenuated psychotic symptoms are often present as a trait marker and predict transition to psychosis, in accordance with the schizotypy framework. However, little is known about the factors modulating the phenotypic expression of schizotypal traits in this population. In this study, we examined the contribution of stressful life events and expected to observe significant associations with positive schizotypy.

Method: 56 participants with 22q11DS (M = 20.53; SD = 6.27) and 30 healthy controls (M = 17.88; SD = 4.39) completed the Schizotypal Personality Questionnaire and the Coddington Life Event Scale. The number and stress load for recent (0-6 months) and less recent (6-12 months) events were computed for each participant.

Results: 73.2% of patients and 86.7% of controls reported at least one stressful life event during the previous year ($\chi^2 = 2.054$, $p = 0.152$). In patients who reported at least one stressful event, stress load for recent events was significantly associated with positive schizotypy ($r = 0.325$, $p = 0.038$), especially suspiciousness ($r = 0.432$, $p = 0.005$), but not with the other schizotypy dimensions. The number of events and stress load of less recent events were unrelated to schizotypy level. In controls, all the associations were statistically non-significant.

Conclusions: This study suggests that the interaction between a genetic liability trait and environmental stress contributes to explain increased risk for psychosis in this population. Implications concerning risk to transition will be discussed.

Talk 3

Schizotypal Traits and Neurocognitive Functioning in a Community-Derived Sample of Adolescents

Eduardo Fonseca-Pedrero^{1,2,3}, Javier Ortuño-Sierra¹, Alicia Pérez de Albeniz¹, Rebeca Aritio-Solana¹, Laura Pérez-Gutiérrez¹

¹Department of Educational Sciences, University of La Rioja, Spain,

²Prevention Program for Psychosis (P3), Spain, ³Center for Biomedical Research in the Mental Health Network (CIBERSAM), Spain

The previous literature asks for further work to establish the ideal latent profile of schizotypal features in samples of the general population. Likewise, there has been no in-depth examination about the relationship between schizotypal latent profiles and its relationship with neurocognitive functioning. The main goal of the present study was to explore the latent structure of schizotypal traits in a community-derived sample of adolescents. Moreover, associations with neurocognitive functioning were compared across different latent classes of schizotypal traits. The present study included one thousand students between the ages of 12 and 19. The Oviedo Schizotypy Assessment Questionnaire (ESQUIZO-Q) and the University of Pennsylvania Computerized Neuropsychological Test Battery for children were used. The 1-hour computerized neurocognitive battery included 14 tasks assessing five neurobehavioral domains (executive functions, episodic memory, complex cognition, social cognition, and sensorimotor speed). Using latent profile analysis four latent classes of schizotypal traits were identified. Furthermore, schizotypal traits were associated with neurocognitive domains. Across schizotypal latent profiles different neurocognitive deficits were found, similar to those found in patients with psychosis. The assessment of schizotypal traits, in community settings, and its associations with neurocognitive performance, may help us to enhance the possibility of an early identification of adolescents potentially at risk for psychosis and mental health problems.

Talk 4**Prediction of Psychosis in a Clinical High Risk Sample: Value of Self-Reported Schizotypy Scales**

Rahel Flückiger¹, Stephan Ruhrmann², Martin Debbané^{3,4}, Chantal Michel¹, Daniela Hubl¹, Benno G. Schimmelmann¹, Joachim Klosterkötter², Frauke Schultze-Lutter¹

¹University of Bern, Switzerland, ²University of Cologne, Germany, ³University of Geneva, Switzerland, ⁴University College London, UK

Schizotypy is considered an indicator of psychosis-proneness and, therefore, a precursor to schizophrenia-spectrum psychosis. In early detection of psychosis, the widely used ultra-high risk criteria refer to the positive features of schizotypy and schizotypal personality disorders (SPD). In clinical high risk (CHR) samples, self-reported or clinically assessed SPD, notably lack of close friends, was suggested to facilitate prediction of psychosis. In community samples, self-reported schizotypy was mainly psychometrically assessed using the four Wisconsin Schizotypy Scales (WSS), and, especially, the positive schizotypy dimension was consistently predictive of psychosis. Psychometrically assessed schizotypy, however, has not yet been studied as a potential predictor of psychosis in CHR samples. To bridge this gap, we studied the psychosis-predictive value of three WSS and their association with a CHR state in a clinical sample. One-hundred and twenty-eight patients (23 ± 7 years; 81% considered as CHR) of two early detection services were followed up for 12–101 months. Within 48 months, 36 (28.1%) converted to psychosis. Only “Physical Anhedonia” was associated with a CHR state, and high scores of “Physical Anhedonia” were predictive of conversion in conjunction with a CHR state. “Physical Anhedonia” rather than positive schizotypy scales might separate future converters from non-converters in clinical samples phenomenologically already presenting a more extreme range of the psychosis continuum. Thus, given their reported psychosis-predictive value in non-clinical samples psychometric schizotypy measures in general might be useful for initial screening of psychosis-proneness in the community, while “Physical Anhedonia” might be particularly useful in CHR samples.

Symposium Session 30

Saturday, October 22, 2:45–4:15 p.m., Washington A

The Use of Virtual Reality and Phone Apps in the Assessment and Treatment of Psychosis

Chair: Lucia Valmaggia¹

Speakers: Maria Rus-Calafell, Mark van der Gaag, Lucia Valmaggia, Roos Pot-Kolder

¹King's College London, Institute of Psychiatry, Psychology and Neuroscience, London, UK

The symposium will present recent evidence of the use of Virtual Reality (VR) and Apps for psychosis research and treatment. Dr Rus-Calafell will discuss how matching the voice of the avatar to mimic auditory hallucinations can help people who hear voices to learn strategies that can generalize to voices in daily life. Prof van der Gaag will talk about the use of TemStem, an App designed to help people cope distressing auditory hallucinations in daily life. Dr Valmaggia will present a new VR English Pub environment designed to help people with psychosis who feel anxious and paranoid in social situations. Finally, Dr Pot-Kolder will show the results of a novel study exploring the effectiveness of VR assisted therapy for the treatment of psychosis.

Talk 1**Examining the Role of Presence in the AVATAR Therapy**

Maria Rus-Calafell^{1,2}, Tom Ward^{1,2}, Philippa Garety^{1,2}, Thomas Craig^{1,2}

¹King's College London, Institute of Psychiatry, Psychology and Neuroscience, London, UK, ²South London and Maudsley NHS Trust, UK

AVATAR therapy is a computer-based intervention which aims to reduce the frequency and severity of auditory verbal hallucinations (AVH). AVATAR uses a Virtual Reality (VR) platform to create and display a human/non-human identity to the patient in order to facilitate a real-time voice “dialogue” between the participant, a computerised representation of their voice and the therapist. This virtual embodiment of the experience is fully achieved by matching the voice of the avatar to the current AVH. This adds even more realism to the experience and seems to be a key aspect of the therapy. We have incorporated an adapted version of the Sense of Presence Questionnaire (Slater, Usoh and Steed, 1995) in order to evaluate the degree of verisimilitude of the experience, the participant's sense of “hearing the voice” and the participant's perception of the avatar as a “voice talking to me”. It is hypothesised that strategies developed in therapy may be more likely to generalize to voices in daily life when the created avatar is high in ecological validity. Data on hallucinations, sense of presence and paranoia in relation to therapy engagement, participant's persecutory thoughts about the avatar and anxiety reduction will be presented and discussed considering previous literature about the relevance of sense of presence in VR interventions for psychosis, but also in relation to specific phenomenological aspects of the AVH.

Talk 2**Reducing Distress and Dysfunction Caused by Auditory Verbal Hallucinations via a Smartphone Application (Temstem)**

Mark van der Gaag^{1,2}, David van den Berg², Alyssa Jongneel², Dorien Scheffers²

¹VU University and EMGO+ Institute for Health and Care Research, Amsterdam, The Netherlands, ²Parnassia Psychiatric Institute, The Hague, Netherlands

Temstem is a Smartphone app aimed to reduce distress by persistent auditory verbal hallucinations. Temstem is making use of three evidence-based interventions: (1) by a verbal task the verbal working memory phonological loop is addressed and this blocks the hearing of voices (behavioural incompatible behaviour); (2) the app reinforces results with compliments that are incompatible with the self-reported themes of the negative self-esteem that the patient has (as in competitive memory training); (3) taxing the auditory working memory during recall of negative auditory memories of the voices who elicit negative emotions, reduces emotionality that is associated to the memories that the voices elicit (as in Eye Movement and Desensitization and Reprocessing therapy). A RCT is now conducted in six sites to examine the effect of the app on distress and dysfunction. Secondary objectives are to investigate the effect of Temstem on frequency and severity of AVH, to determine working mechanisms, to identify predictors and mediators of effects, and to test the usability of Temstem. Preliminary results will be presented.

Talk 3**Come to My Party! Using Virtual Reality to Improve the Assessment and Treatment of Social Performance**

Lucia Valmaggia^{1,2}, Mar Rus-Calafell^{1,2}, Simon Riches^{1,2}, Thomas Craig^{1,2}, Philippa Garety^{1,2}

¹King's College London, Institute of Psychiatry, Psychology and Neuroscience, London, UK, ²South London and Maudsley NHS Trust, London, UK

Building on previous evidence we wanted to investigate whether cognitive (fear of negative evaluation), affective (social distress) and behavioural (social avoidance) components of social performance (CSP) are associated with increased paranoid ideations in a VR social environment. A large general population online survey (N = 609) investigated how trait paranoia relates to CSP and mood. Participants who scored higher (N = 44) and lower (N = 44) in trait paranoia entered a VR party in an English Pub to evaluate the acceptability of the new VR paradigm and the relationship between paranoia and CSP. As hypothesised, trait paranoia was associated with CSP and higher trait paranoia participants reported higher state paranoia and greater negative CSP in VR. The assessment and treatment applications of this new environment for people with psychosis will be presented.

Talk 4**The Effect of Cognitive Behavior Therapy Augmented with Virtual Reality Exposure Therapy on Social Participation in Patients with a Psychotic Disorder (VRETP)**

Roos Pot-Kolder^{1,2}, Wim Veling^{2,3,4}, Chris Geraets³, Philippe Delespaul^{4,5}, Mark van der Gaag^{1,2}

¹Parnassia Psychiatric Institute, The Hague, The Netherlands, ²VU University and EMGO+ Institute for Health and Care Research, Amsterdam, The Netherlands, ³University of Groningen, The Netherlands, ⁴Maastricht University, The Netherlands, ⁵Mondriaan Psychiatric Institute, Maastricht, The Netherlands

Several patients in (partial) remission of a psychotic disorder still avoid social situations because of distrust and anxiety. Avoidance behaviours are an important factor in sustaining social isolation and it can be hard to motivate patients to omit these behaviours in real life. Cognitive Behavior Therapy augmented with Virtual Reality Exposure Therapy (VRETP) has the potential to be an affordable and accessible form of treatment to enhance social participation and wellbeing for patients suffering from paranoia and social withdrawal. The study design is a single blind randomized clinical trial with three-month follow-up. The VRETP treatment consists of sixteen treatment sessions of sixty minutes each, within an eight-week timeframe. Social participation was measured with the PsyMate Experience Sampling Method. One hundred and sixteen participants were included in the study. Fifty-eight participant participants received the VRETP treatment in addition to treatment as usual (TAU). The other fifty-eight participant received only TAU during the study. Preliminary results show feelings of paranoia in daily life social situations were significantly reduced for participants that received the VRETP treatment. More results will be ready for IEPA in October. VRETP appears to be an effective treatment for reducing feelings of paranoia in social situations for patients with a psychotic disorder. Limitations of the results and the study will be discussed.

Question and Answer Period

Discussant: Wim Veling, University of Groningen, The Netherlands

**Symposium Session 31
Saturday, October 22,
2:45–4:15 p.m., Washington B****Individual Placement and Support: The Importance of Integrating Supported Education in Early Intervention**

Chair: Luana R Turner¹

Speakers: Eóin Killackey, Jaap van Weeghel, Wenche ten Velden Hegelstad, Luana R Turner

¹Department of Psychiatry and Biobehavioral Sciences, Semel Institute for Neuroscience and Human Behavior, University of California, Los Angeles, CA, USA

The goal of gaining and maintaining independence lies at the core of every individual's identity and self-esteem. A key component of this dynamic is employment, however education is innately tied to this process. The most evidenced-based model of supported employment is the Individual Placement and Support Model (IPS); though little research has been conducted on the integration and value of an IPS fidelity scale that includes supported education. This symposium will explore the importance of an integrated scale, and how this scale can assist in identifying the challenges, needs, and accommodations of clients early on to improve the likelihood of academic and employment success. The symposium will also report on the results of using an adapted IPS fidelity scale (AIPSFs) in two randomized controlled trials (RCT's) across 9 early intervention teams in the Netherlands and 2 teams in Norway. This symposium will describe how researchers from Australia, the Netherlands, Norway, and the U. S. have created an AIPSFs integrating supported education, the process of coordinating these efforts across continents, and how the systems in each country contribute to the diversity of the adapted scale. Furthermore, this symposium aims to demonstrate the need for an adapted fidelity scale that utilizes the existing IPS scale as the foundation, and that IPS workers should be trained to deliver supported education and employment as integrated services to their clients. In summary, empirical findings and clinical issues regarding the need for an adapted IPS fidelity scale integrating supported education in early intervention will be discussed.

Talk 1

Starting Fires, Not Filling Buckets: The Importance of Education in the Vocational Recovery of Young People with First Episodes Psychosis

Eóin Killackey^{1,2}

¹Orygen, The National Centre of Excellence in Youth Mental Health, Parkville, VIC, Australia, ²Centre for Youth Mental Health, The University of Melbourne, Australia

Psychosis inflicts much harm on those who experience it. Of these, vocational disability that can accrue to individuals is particularly costly, personally, societally and economically. The last 25 years has seen the development of evidence based vocational recovery interventions for people with psychotic illness, particularly the Individual Placement and Support (IPS) form of Supported Employment. However, the majority of the development of these interventions has been in populations with long-standing illness. Consequently, most of the outcomes sought have been employment related. Over the last 10 years there has been a growing application of IPS to young people with first episode psychosis. For these young people educational outcomes are as valued as employment outcomes. This is for two key reasons. Firstly, for this group whose vocational aspirations are as yet undiminished by their illness, the completion of education and training gives the greatest chance of engaging with a hoped-for career instead of just getting a job. Secondly, increased levels of education will be protective against the increasing automation of entry-level jobs. Reviews show however, that IPS is as yet not producing the same advantages in educational outcomes that it produces for employment outcomes. One reason for this may be that IPS and the IPS fidelity scale is a priori directed to employment. This presentation will discuss education in the context of vocational recovery, adaptations to IPS that are required to more effectively promote education and the need to more accurately measure the fidelity of aspects of IPS targeted to educational outcomes.

Talk 2

Adding a Supported Education Fidelity Scale to Individual Placement and Support (IPS) Practices for Persons with a First Episode of Psychosis in The Netherlands

Jaap van Weeghel^{1,2}, Isis van Soest¹, Daniëlle van Duin¹

¹Kenniscentrum Phrenos, ²Tilburg University, The Netherlands

Objective: In The Netherlands IPS services of first episode psychosis programs have increasingly included Supported Education (SEd). The objective of this research project is a) to develop a complementary SEd scale for IPS practices serving persons with early psychosis and b) to integrate this scale addressing education supports with the existing IPS fidelity scale addressing employment supports.

Methods: A preliminary IPS SEd fidelity scale is developed by means of studying the literature on SEd and IPS model fidelity, consulting Dutch experts on this subject, and conducting a focus group of IPS practitioners and IPS trainers. Within the context of a multisite RCT on IPS practices in nine early intervention teams, each serving 100-150 clients, the IPS SEd scale is administered at baseline and at one-year follow up. IPS trainers and practitioners are interviewed discussing the validity and feasibility of the scale.

Results: At baseline (September 2015) eight teams scored 'fair fidelity' and one team 'good fidelity' on the integrated IPS fidelity scale. No systematic differences were found between scores on the employment and education items.

Discussion: At baseline, the participating teams had just started implementing IPS. It is yet to be seen whether these teams, according to the fidelity assessment at one-year follow-up (September 2016), will have made progress on the employment part, the education part, or on both parts of their IPS practices. Also the feasibility and validity of the SEd scale will be discussed, based on the experiences of the IPS practitioners, trainers and researchers.

Talk 3

Earning and Learning: Two Sides of the Same Coin. Testing of an Integrated IPS Fidelity Scale for Education and Employment in Norway

Wenche ten Velden Hegelstad¹, Kristin Hatløy¹, Lena Heitmann², Jan Olav Johannessen¹

¹Stavanger University Hospital, Regional Centre for Clinical Research in Psychosis, Norway, ²Stavanger University Hospital, Division of Psychiatry, Job Prescription/ School Prescription, Norway

Purpose: Finishing school is important for social participation and later employment, but may be impeded by mental illness. An IPS intervention for employment was expanded to help young people with severe mental illness or ultra high-risk states maintain or gain education. The purposes of the presented project were to test the utility of an adapted and integrated fidelity scale for supported education and employment, and to evaluate the integrated intervention.

Material and methods: A multi-site international work group (USA, Australia, UK, the Netherlands, Norway) adapted the IPS fidelity scale by Bond et al(1) to integrate supported employment and education. An external expert rated the intervention using observations of client contacts and methods of work, and interviews with staff, organization leadership, and collaborators in vocational and educational services. Re-testing will be conducted in April 2017, and Scandinavian sites invited to participate.

Results: Fidelity ratings will be presented. Preliminary results indicate satisfactory fidelity. There are however some discrepancies from standard IPS: 1) The IPS workers do not serve clients from designated mental health care teams exclusively 2) Frequency of contacts with educational services are flexible as opposed to fixed. Strengths are rapid enrolment and start of collaboration with educational/employment facilities, close collaboration with treating clinicians, and integration with mental health care.

Conclusion: The integrated scale is promising as a tool for ensuring high-quality delivery of an integrated education/employment intervention. Assisting young people with severe mental illness pursue educational goals provides an opportunity to prevent later unemployment and social exclusion.

Talk 4

Supported Education as a Key Early Intervention: The Path Toward Integration of Services

Luana R Turner

Department of Psychiatry and Biobehavioral Sciences, Semel Institute for Neuroscience and Human Behavior, University of California, Los Angeles, USA

Supported employment has become an integral and poignant component of recovery. However, supported education services are often viewed as a separate intervention. As the mental health field continues to appropriately increase focus on early interventions, it is important to view supported education as a natural expansion of the supported employment intervention. The Individual Placement and Support (IPS) model offers excellent fidelity as a solid base to integrate educational services. This presentation will report on these topics, current supported education services, programs that adapted IPS for supported education, and the development of the adapted IPS fidelity scale (AIPSFS). Furthermore, this presentation will explore the benefits of using supported education with first-episode clients as well as prodromal populations and children under the age of 18. This presentation will also report on the advantages of utilizing a fidelity scale that distinguishes the differences between the interventions of supported education and employment, yet still provides for an integrative scoring system. Lastly, this presentation will discuss the process of the AIPSFS project, including the benefits and challenges of working with colleagues across the globe, and conceptualizing a model that meets the diversity of the different educational systems around the world.

Question and Answer Period

Discussant: Luana R Turner, *Department of Psychiatry and Biobehavioral Sciences, Semel Institute for Neuroscience and Human Behavior, University of California, Los Angeles, USA*

Symposium Session 32

Saturday, October 22, 2:45–4:15 p.m., Manzoni

The US Generation of Early Psychosis Intervention Services: What is Coordinated Specialty Care and How Does It Compare to Other International Initiatives?

Chair: Piper Meyer-Kalos¹

Speakers: Piper Meyer-Kalos, Iruma Bello, Tamara Sale, Merete Nordentoft

¹*University of Minnesota, Minnesota Center for Chemical and Mental Health, MN, USA*

Purpose: The US has developed a new model of care to support the development of early psychosis treatment programs across the country. This new model is called Coordinated Specialty Care (CSC). CSC includes low doses of antipsychotic medications, cognitive-behavioural and recovery-oriented psychotherapy, family education and support, and vocational and educational rehabilitation to promote clinical and functional recovery and prevent disability among persons with first episode psychosis. The National Institute of Mental Health (NIMH) funded the development and testing of CSC programs across the US. Findings from the two Recovery After Initial Schizophrenia Episode (RAISE) research initiatives have suggested that these programs can be implemented in routine US mental health settings. While there are many shared CSC components in US and international first episode programs, the lack of a national health system has

had a significant impact on the dissemination and uptake of these programs in the US.

Methods: This symposium will describe three major CSC models currently being implemented in the US: NAVIGATE, OnTrackNY, and Early Assessment and Support Alliance (EASA). Each presentation will discuss how each program incorporates the core components of the team based, multi-component CSC model and current efforts to disseminate CSC.

Results: Each program will review results from the dissemination and training efforts and describe the challenges of dissemination in the US.

Conclusion: The CSC model presentations will conclude with a discussion panel of four international experts who will respond to the US experience of developing early intervention services in comparison to international efforts.

Talk 1

NAVIGATE: An Overview of the Implementation and Dissemination Strategies in Routine Settings for a Team-Based, Comprehensive Intervention for First Episode Psychosis

Piper Meyer-Kalos¹, Shirley Glynn², Susan Gingerich³, Kim Mueser⁴

¹*Minnesota Center for Chemical and Mental Health, University of Minnesota, MN, USA*, ²*Research Psychologist at Semel Institute of Neuroscience and Human Behavior University of California, Los Angeles, USA*, ³*NAVIGATE Training Coordinator*, ⁴*Center for Psychiatric Rehabilitation, Boston University, MA, USA*

Purpose: NAVIGATE is an example of an evidence-based coordinated specialty care (CSC) model. The NAVIGATE team works together to provide four core services: individualized medication management, family education (FE), individual resiliency training (IRT), and supported employment and education (SEE). In NAVIGATE, treatment is guided by three conceptual frameworks that include the recovery model, the stress-vulnerability model, and the field of psychiatric rehabilitation.

Methods: Since the RAISE-ETP study has concluded, the NAVIGATE model has been disseminated as part of a national effort to increase early intervention services. The training and dissemination model for NAVIGATE is designed to foster the development of the core skills utilized in all treatment components including shared decision making, strengths and resiliency, psychoeducation, and collaboration with natural supports.

Results: In this presentation we will describe the NAVIGATE program and discuss our training and implementation model. We will present results from the dissemination of NAVIGATE in 11 programs in 8 states and include recommendations for dissemination in the US. To date, team training has been done in-person and followed up by regular role-specific consultation calls for at least one year.

Conclusion: In NAVIGATE, we provide a flexible and supportive approach to training and implementation that addresses readiness to start a first episode program, development of expertise in treatment for first episode psychosis, and skill development for each role on the team as well as promoting the sustainability of services.

Talk 2

OnTrackNY: Training Strategy for Implementing a Coordinated Specialty Care Service Model in the USA

Iruma Bello^{1,2}, Lisa Dixon^{1,2}, Liza Watkins¹, Tom Smith¹, Rufina Lee³, Gary Scannevin¹, Ilana Nossel^{1,2}, Lloyd Sederer⁴

¹New York State Psychiatric Institute, New York, NY, USA, ²Columbia University Medical Center, New York, NY, USA, ³Silberman School of Social Work at Hunter College, City University of New York, NY, USA, ⁴Office of Mental Health, New York, NY, USA

Purpose: This presentation will discuss OnTrackNY's training strategy for implementing coordinated specialty care services. OnTrackNY's consultation activities begin with pre-implementation planning (e.g., embedding a team within an agency, mapping existing policies and procedures, addressing challenges across child/adult service divides, hiring staff) and continue through model implementation.

Methods: Training consists of a flexible strategy delivered by a centralized team of experts. A three-day in person training introduces providers to the service model and its component parts. Technical assistance is continued through collaborative role-based calls, monthly care consultation calls, and special topics requested by trainees (e.g., violence risk, LGBT issues). This is combined with a web-based learning management system that allows for self-paced learning through webinars and supplementary materials. New York based teams receive a robust and continuous training package. The intensity of training activities for other states is varied and lasts at least one year.

Results: Twelve teams have been trained across diverse communities in New York. The state's effort is currently expanding to train 8 additional teams. Across the US, 12 states have been trained (22 teams) in addition to Puerto Rico and the Pacific Jurisdictions. A majority of feedback forms (74%-93%, $n = 485$) submitted by for the in-person training sessions reflect that trainees strongly agreed that the material presented was useful and was presented in an engaging manner by knowledgeable and skilful presenters.

Conclusion: OnTrackNY's comprehensive and adaptive training strategy has been successful in training providers across varied demographic settings enabling the effective implementation of coordinated specialty care services.

Talk 3

Integrating Coordinated Specialty Care in the U.S.: Oregon's Experience

Tamara Sale¹, Ryan Melton¹, Katherine Hayden-Lewis¹, Craigan Usher²

¹Portland State University, Portland, Oregon, ²Oregon Health & Science University, Portland, Oregon

Purpose: Oregon's early leadership in integrating preventive and evidence-based strategies into health care reform resulted in the first systematic adoption of early psychosis intervention within the U.S. public mental health system in 2001.

Methods: Statewide dissemination of Oregon's Early Assessment and Support Alliance (EASA) began in 2008 and attempted to realign financial incentives toward population-based early psychosis services.

Results: Local EASA teams provide all of the elements of Coordinated Specialty Care to residents regardless of insurance coverage, serving over 400 individuals and families per year. EASA's early implementation evolved under a governance structure consisting of providers, service participants and funders, who defined the purpose and underlying problems.

Conclusion: As a result, EASA's implementation framework integrates the perspective of individuals with lived experience of psychosis as well as strategic and operational concerns, and attempts to maximize the impact of evolving research on systems and participant wellbeing while recognizing the limitations of research. The EASA Center for

Excellence facilitates a National Learning Collaborative representing fifteen diverse states, works with RAISE consultants and other national trainers, and participates in the development of the EPINET "learning healthcare system" focused on early psychosis. EASA focuses on developing and supporting leadership, organizational capacity, and clinical capacity to implement Coordinated Specialty Care.

Talk 4

Panel Discussion from International Experts in Response to the US Experience Disseminating Treatment for First Episode Psychosis

Merete Nordentoft¹, Eóin Kilackey², Max Birchwood³, Donald Addington⁴

¹Professor, chief Psychiatrist, University of Copenhagen, Mental Health Centre Copenhagen, Denmark, ²Orygen, The National Centre of Excellence in Youth Mental Health Centre for Youth Mental Health; The University of Melbourne, Parkville, VIC, Australia, ³School of Psychology, University of Birmingham, Professor of Youth Mental Health Clinical Director, YouthSpace Mental Health Service, Birmingham and Solihull Mental Health Foundation Trust, ⁴Professor Department of Psychiatry, Member Mathison Centre for Mental Health Research and Education, University of Calgary, Alberta, Canada

Purpose: This panel discussion will focus on comparing and contrasting the US experience with training and dissemination of a coordinated specialty care (CSC) model for first episode psychosis treatment with the international experience of developing early intervention services.

Methods: Four international experts in early intervention services will share their feedback in response to the descriptions of the three US programs: NAVIGATE, OnTrackNY, and Early Assessment and Support Alliance (EASA).

Results: Experts will describe the similarities and differences to the development of first episode programs outside of a national health system. Experts will also respond to the common challenges in training and dissemination across the US first episode training programs.

Conclusion: The development of first episode psychosis programs in the US is uniquely different from many other international programs. Sharing information about the training and dissemination efforts may enhance the sustainability of first episode psychosis programs and lead to better outcomes for persons with first episode psychosis and their families.

Symposium Session 33

Saturday, October 22, 2:45–4:15 p.m., Foscolo

Oxidative Stress in Early Psychosis, from Mechanisms to Interventions

Chair: Arjen Sutterland¹, Co-Chair: Philipp Baumann²

Speakers: Daniella Dwir, Arjen L. Sutterland, Marie-Odile Krebs, Philipp Baumann

¹University of Amsterdam, The Netherlands, ²Lausanne University Hospital (CHUV), Switzerland

In this symposium the role of oxidative stress in early psychosis will be highlighted, with latest results from several studies. Different approaches will be presented, whereby the relation of oxidative stress with neuroinflammation, advanced glycation endproducts and common pathological findings in psychosis is demonstrated. Firstly, Daniella Dwir will introduce the concept of oxidative stress and the role of the receptor for advanced glycation endproducts in the interaction between oxidative stress and neuroinflammation. Data indicates that redox dysregulation can be a potential trigger of structural and morphological impairments in the adult brain similar to schizophrenia. Next, Arjen Sutterland will elucidate how measuring accumulation of advanced glycation endproducts non-invasively in early psychosis subjects can be an indication for increased oxidative stress. Correlations with clinical variables, cardiovascular risk factors and peripheral markers of inflammation and oxidative stress are presented. Consequences for current treatment strategies are discussed. Then, Marie-Odile Krebs will demonstrate that subjects with ultra high risk for psychosis who convert to psychosis differ from non-converters in methylation patterns of their DNA. The epigenetic changes in converters occur in pathways relevant for psychosis, including oxidative stress regulation, axon guidance and inflammatory pathways. Lastly, Philipp Baumann will present the relation of oxidative stress with neuropathological findings in vivo in psychosis, whereby the integrity of the fornix-hippocampus circuits is studied with neuroimaging, showing that its impairment is linked to peripheral redox dysregulation in early psychosis. Lieuwe de Haan will discuss the implications for clinical practice, possibilities for stratification and its relevance to future interventions.

Talk 1

Involvement of the Receptor for Advanced Glycation End-product (RAGE) in the Interaction Between Redox Dysregulation and Neuroinflammation: Relevance for Schizophrenia

Daniella Dwir, Jan-Harry Cabungcal, Pascal Steullet, Michel Cuénod, Kim Q Do

Lausanne University Hospital (CHUV), Switzerland

Growing bodies of evidences show the involvement of a redox and inflammatory dysregulation in the pathophysiology of schizophrenia (SZ). For instance, decreased glutathione (GSH) levels, an important redox regulator, have repeatedly been demonstrated. It has been suggested that oxidative stress and inflammation occurring at a critical period may affect neurons vulnerable to elevated oxidative insults, such as parvalbumin-expressing interneurons (PVI), which circuit is impaired in SZ. While several mechanisms have been proposed for oxidative stress and inflammation interaction, we focus on the role of the Receptor for Advanced Glycation End-product (RAGE). RAGE is a promising candidate as its ligands are produced in both oxidative stress and inflammatory conditions. RAGE activation leads to further reactive oxygen species production and inflammatory pathway activation. Interestingly, AGEs and S100B, two major ligands of RAGE

were shown to be increased in SZ patients. Our results showed that RAGE shedding by MMP9 was involved in maintaining a vicious cycle of oxidative stress and inflammation in early development in a mouse model of GSH deficit that shows SZ related phenotype. These mice show decreased PVI/PNN, increased oxidative stress and microglia activation in anterior cingulate cortex in adulthood after an additional oxidative stress in early postnatal days, which could be reversed by RAGE shedding inhibition. We propose that an interaction between redox dysregulation and pro-inflammatory condition via RAGE and MMP9 in early developmental stages is a potential trigger of structural and morphological impairments in adult brain. Therefore, RAGE/MMP9 pathway could be a new promising target for drug development.

Talk 2

Advanced Glycation Endproducts and Cardiovascular Risk in Relation to Inflammation and Oxidative Stress in Recent Onset Psychosis

Arjen L. Sutterland¹, Julia M. Hagen¹, Maarten Koeter¹, Rene Lutter¹, Dan Cohen², Lieuwe de Haan¹

¹University of Amsterdam, The Netherlands, ²Mental Health Service North-Holland North, The Netherlands

Profoundly increased mortality rates in schizophrenia, largely caused by a higher risk and earlier onset of cardiovascular disease, remain a major challenge. During human life Advanced Glycation Endproducts (AGEs) accumulate, of which the concentration is strongly linked to cardiovascular mortality. AGEs accumulation can be increased by several pathways, including inflammation and oxidative stress. A case control study was performed including 111 patients with a recent onset psychosis, 135 controls from a validation cohort and a group of 321 healthy controls. Main outcome parameters were levels of AGEs measured through skin autofluorescence. AGEs were compared with healthy controls controlling for age, gender and smoking. Correlations of AGEs with well-known cardiovascular risk factors, clinical variables, as well as inflammatory factors and level of oxidative stress measured in plasma were analysed by hierarchical linear regression analyses. An AGE measurement was possible in 77.4%. AGEs were elevated by 15.1% in recent onset psychosis compared to healthy controls ($P < .001$), corresponding to an increased accumulation of AGEs normally occurring in over 10 years. Duration of disease, duration of antipsychotic treatment and cumulative exposure to antipsychotics correlated with AGE levels ($p = 0.008, 0.009$ and 0.023 respectively). Correlations with inflammatory and oxidative stress markers will be presented. We conclude that in patients suffering from recent onset psychosis increased AGE levels compared with healthy controls are already present. These findings argue for an earlier treatment of cardiovascular risk factors and possibly conservative dosing strategies of antipsychotics in schizophrenia. Mechanisms how AGEs accumulation is raised in psychosis needs to be explored further.

Talk 3

Methylyomic Changes During Conversion to Psychosis

Marie-Odile Krebs^{1,2}, Oussama Kebir^{1,2}, Boris Chaumette^{1,2}, Fabrice Rivollier^{1,2}, Federico Miozzo³, Sylvie Provost⁴, Marion Plaze^{1,2}, The ICAAR Team, Raphaël Gaillard^{1,2}, Valérie Mezger³, Marie-Pierre Dube⁴

¹Université Paris Descartes, France, ²Centre Hospitalier Sainte-Anne, Paris, France, ³Université Paris Diderot, France, ⁴Université de Montréal, Canada

The onset of psychosis is the consequence of complex interactions between genetic vulnerability to psychosis and response to environmental and/or maturational changes. Epigenetics is hypothesized to mediate the interplay between genes and environment leading to the onset of psychosis. We believe we performed the first longitudinal prospective study of genomic DNA methylation during psychotic transition in help-seeking young individuals referred to a specialized outpatient unit for early detection of psychosis and enrolled in a 1-year follow-up. We used Infinium HumanMethylation450 BeadChip array after bisulfite conversion and analyzed longitudinal variations in methylation at 411 947 cytosine-phosphate-guanine (CpG) sites. Conversion to psychosis was associated with specific methylation changes. Changes in DNA methylation were significantly different between converters and non-converters in two regions: one located in 1q21.1 and a cluster of six CpG located in GSTM5 gene promoter. Methylation data were confirmed by pyrosequencing in the same population. The 100 top CpGs associated with conversion to psychosis were subjected to exploratory analyses. Cluster analysis showed that the top CpG sites correctly distinguished between converters and non-converters. In this first study of methylation during conversion to psychosis, we found that alterations preferentially occurred in gene promoters and pathways relevant for psychosis, including oxidative stress regulation, axon guidance and inflammatory pathways. Although independent replications are warranted to reach definitive conclusions, these results already support that longitudinal variations in DNA methylation may reflect the biological mechanisms that precipitate some prodromal individuals into full-blown psychosis, under the influence of environmental factors and maturational processes at adolescence.

Talk 4

Impaired Fornix-hippocampus Integrity is Linked to Peripheral Glutathione Peroxidase in Early Psychosis

Phillipp Baumann¹, Alessandra Griffo^{1,2}, Margot Fournier¹, Philippe Golay¹, Carina Ferrari¹, Alameda Luis¹, Michel Cuenod¹, Jean-Philippe Thiran^{1,2}, Patric Hagmann^{1,2}, Kim Q. Do¹, Philippe Conus¹

¹Lausanne University Hospital (CHUV), Switzerland, ²Signal Processing Laboratory (LTSS) Lausanne, Switzerland

Different lines of evidence implicate the fornix-hippocampus circuit in schizophrenia. Given that this circuit has not been extensively investigated in early phase psychosis, the underlying mechanisms affecting the circuit remain unknown. The hippocampus and fornix are vulnerable to oxidative stress at peripuberty in a glutathione (GSH; main non-protein antioxidant) deficient animal model (Corcoba et al., 2015; Steullet et al., 2010). The purposes of the current study were to assess the integrity of the fornix-hippocampus circuit in early psychosis patients (EP), and to study its relationship with peripheral redox markers. 42 EP patients (age 25.0 ± 5.4) having met threshold criteria for psychosis, as defined by the CAARMS were recruited from TIPP, an integrated early psychosis program in Switzerland. 42 gender and age-matched healthy controls were also recruited. Diffusion Spectrum Imaging and T1-weighted Magnetic Resonance Imaging (MRI) were used to assess fornix and hippocampus. Generalized

fractional anisotropy (gFA) and volumetric properties were used to measure fornix and hippocampal integrity respectively. Correlation analysis was used to quantify the relationship of gFA in the fornix and hippocampal volume, with blood GSH levels and glutathione peroxidase (GPx) activity. Patients compared to controls exhibited lower gFA in the fornix as well as smaller volume in the hippocampus. In EP but not in controls, smaller hippocampal volume was associated with high GPx activity. Disruption of the fornix-hippocampus circuit is already present in the early stages of psychosis. Higher blood GPx activity is associated with smaller hippocampal volume, which may support a role of oxidative stress in disease mechanisms.

Question and Answer Period

Discussant: Lieuwe de Haan, University of Amsterdam, The Netherlands

Symposium Session 34 Saturday, October 22, 2:45–4:15 pm, Parini

A Cautionary Tale or Breach of Promise? The Ups and Downs of Resourcing, Development, Dissemination and Sustaining of Early Intervention Teams in Australia & The UK & Canada

Chair: Alan Rosen¹, Co-Chair: Peter Byrne²

Speakers: Alan Rosen, Patrick D. McGorry, Roger Gurr, Peter Byrne
¹Brain & Mind Centre University of Sydney, Illawarra Institute of Mental Health University of Wollongong, Australia, ²Royal College of Psychiatrists UK, Homerton University Hospital London, UK

Australia's research, clinical and affected community have been successful until recently in nationally innovating and disseminating Early Intervention services for young people with Psychosis and other psychiatric disorders. Youth friendly "headspace" centres provide a one-stop-shop approach to assessment of troubled young people, then connecting them with a range of mental health, substance use and physical health services. They are now widespread and they have been the launching pad of a pilot program in needy regions in each state and territory of specific formerly "headspace" managed young people with psychosis early intervention (hYEPP) teams. These highly evidence based teams were brought in on the basis of bipartisan policy only a few years ago. They are now being told they face a step-wise dismantling by the Australian Conservative Federal government, without giving them a proper chance to develop and bloom, and demonstrate the expected positive outcomes. This will lead to many sackings of committed and skilled team staff and a dashing of the much more hopeful expectations of many young individuals and their families. Similar processes have been observed internationally, particularly in the UK in the wake of the shrinkage of the NHS on the watch of the current Conservative government. A discussion will ensue regarding how we can better anticipate, prevent, or ameliorate these cycles of innovation, rigorous outcome research, nationally widespread piloting and then wholesale political undoing, and how to ensure that EIP teams have adequate opportunities to become stabilized, regionally disseminated and threaded nationally throughout all mental health services.

Talk 1

Introductory Narrative: The Story So Far

Alan Rosen

University of Sydney, Sydney, Australia

A national network of highly evidence based teams, piloting early intervention in psychosis in each state were implemented on the basis of bipartisan policy only a few years ago. Such teams have been demonstrated to be highly cost-effective over medium to long-term studies. They have also been national pioneers in extending continuity of care in an EIP team for up to 5 years, employing of mental health clinicians and peer workers in NGO sector-run teams, demonstrating the diversifying of the provider market, and planning multi-site trials of potentially synergistic approaches such as Open Dialogue. They now are to be dismantled stepwise by the Australian Conservative Federal Government, without giving them any chance to develop, stabilize, and demonstrate the expected positive outcomes. The existing resources will be sprinkled lightly over 31 Primary Health Networks, which will redeploy them variably, as they have no experience in this field, and very different priorities. Inevitably, these resources will be absorbed for other purposes, and shrunk even further, with the Government shifting the blame to the PHN's, and none of these coherent EIP services will remain. This will destroy the fidelity to the evidence based EIP model, which relies on a manageable geographical catchment area for 7 day home visiting, and expert team staff, who will lose their jobs. Several hundreds of very troubled young people and their families will have expectations of more intensive and appropriate care dashed, dumped onto the underfunded local state services, which will be unable to serve them effectively.

Talk 2

International Comparisons in Disseminating and Stabilizing Early Intervention in Psychosis

Patrick D. McGorry, M.D., Ph.D.

Orygen Youth Mental Health & University of Melbourne, Parkville, VIC, Australia

A contextual analysis of the way this happened and the way forward for government, mental health services, primary health networks etc. and whether a pre-election campaign and an effective Federal opposition was able to make a difference. How should we set the balance between early intervention of psychosis and other disorders? What level of resourcing will it really require? What sequencing should occur between completing model development and pilots in each state jurisdiction and widespread dissemination? How do we stop this political lurching and destabilization happening again? Similar processes have been observed internationally, particularly in the UK in the wake of the shrinkage of the NHS on the watch of the current Conservative government. What has been achieved and what have Government and NHS administrations undone? What can be done from here and what are the lessons? At the same time, more countries are demonstrating very good outcomes in national networks of local services eg RAISE study in USA, Scandinavia, Canada, Netherlands, Ireland etc.

Talk 3

Working with Governments, Public, Private and NGO Sectors

Roger Gurr

Western Sydney University, Sydney, Australia

How has it been possible to successfully combine the efforts of public, not-for-profit (NGO) and fee-for? service sectors in the common enterprise of establishing regional services for Early Intervention in Psychosis. They combine an ultra-high-risk monitoring, therapy and support team, an acute 7 day mobile outreach team and an assertive community outreach team for persistent psychoses in young people? At The Macro Level: How can we create an optimal governmental and commissioning environment for piloting, regionally disseminating and sustaining cost-effective evidence based components such as Early Intervention in Psychosis teams? Can a federated, or even unitary, national system succeed in supporting and stabilizing such mental health reforms? Or for mental health services are such pressing needs easily turned into political footballs, kicking the responsibility and the blame for the failure to systemize them between different political complexions, levels of government and funding bodies? How can we do better than this nationally?

Talk 4

The UK Experience

Peter Byrne

London Hospital, London, UK

Service users' high preferences for all three services were not enough to save assertive outreach teams from cuts that followed the 2008 global economic crisis. By virtue of expediency, in the face of sustained cuts to the number of inpatient beds available, home treatment teams have survived across England: the levels of risk they assume are reflected in falling inpatient suicide rates but rising death rates among their clients. Having shown the most evidence of efficacy, the smartest economic modelling and sustained flexibility EIP services have mostly held on to their funding in a climate where England's MH services have lost 8% in real terms. There is a growing national awareness of MH stigma and its need for "parity of esteem" with physical healthcare services. This has mostly led to a cross-party consensus that MH innovative services like EIP should be protected. But an ideological drive towards competition between services (as opposed to competition to fight misery or deliver the best outcomes for people) may pitch younger people's services against EIP that has come to mean 18-36 services. The onus is on all of us to keep helping our service users and carers, proving the best outcomes, and advocating for EI services.

Question and Answer Period

Discussant: Katherine Boydell, *Black Dog Institute University of New South Wales Australia, and University of Toronto, Canada*